The Cerebral Organization of Absolute Pitch within the Framework of Music and Speech

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Contents

I. Summary

In cognitive neuroscience research the question whether musical expertise affects or even facilitates language processing has been increasingly addressed in recent years. The assumption that language acquisition and ability of absolute pitch (AP) develop in parallel, let suggest that AP ability might be regarded as a model of cortical plasticity for deliberate practice and musicianship. From a neurophysiological point of view AP has been shown to be associated with morphological changes and adaptations in the planum temporale (PT), which is also considered to be involved in speech perception processes. However, a direct link between speech processing and AP has hitherto not been addressed. Insofar in this thesis I introduce two different perspectives on this issue: first, an experiment with functional magnetic resonance imaging (fMRI) in which the presence of meaning and intonation in German spoken language were systematically varied; second, an analysis of diffusion tensor imaging (DTI) data in musicians with AP, which enables to measure neural connectivity in speech relevant white matter pathways as a function of musical expertise.

The results let conclude that structural and functional alterations due to musicianship do not only manifest in exceptional acuity of music processing, but affects speech processing in that sense that AP represents a comprehensive analytical proficiency for acoustic signal decoding.

II. Zusammenfassung

Im Bereich der kognitiven Neurowissenschaften gewinnt die Frage ob eine musikalische Expertise positive Auswirkungen auf die Verarbeitung von Sprache haben könnte, zunehmend an Wichtigkeit. Aus neurophysiologischer Sicht konnte das absolute Gehör mit hirnmorphologischen Adaptionen – speziell des Planum Temporale (PT) – in Verbindung gebracht werden. Da diese Struktur aber offenbar einen wichtigen Beitrag zur basalen Sprachverarbeitung leistet, stellt sich die Frage inwiefern diese mit der Fähigkeit des absoluten Gehörs im Zusammenhang stehen könnte. Insofern stellt die vorliegende wissenschaftliche Arbeit im Rahmen meiner Dissertation den ersten Versuch dar, sich mit diesem Themenfeld zu befassen.

Zur Untersuchung dieser Fragestellung dienten die folgenden beiden methodischen Ansätze: Erstens, in einer experimentellen Situation wurden bei gesprochener Sprache prosodische und lexikalische Informationen systematisch manipuliert, während die sich ausbreitende Hirnaktivität mittels funktioneller Magnet-resonanztomographie aufgezeichnet wurde; zweitens, mittels Diffusions-Tensor Magnetresonanztomographie wurden zum ersten Mal Musiker mit absolutem Gehör gemessen, was die Möglichkeit eröffnete, neuronale Konnektivität als Funktion musikalischer Expertise in sprachrelevanten Nervenfaserbündeln zu studieren.

Aus den vorliegenden Resultaten lässt sich schlussfolgern, dass sich strukturelle und funktionelle Plastizität bei Musikern nicht nur – wie hinlänglich bekannt - bei der Verarbeitung von Musik äussert, sondern darüber hinaus die Sprachverarbeitung von Musikern mit absolutem Gehör dahingehend beeinflusst, dass sich dieses als ausserordentliche analytische Fähigkeit im Hinblick auf akustische Signaldekodierung begreifen lässt.

1. Introduction

1.1. Absolute Pitch

“Absolute pitch” (AP) is a very rare phenomenon among professional musicians, enabling them to identify tones without the aid of any reference tone. In terms of cognitive music psychology, AP could be characterized as the ability to distinguish and identify one salient quality (the pitch chroma) from a number of other perceptual attributes (Levitin & Zatorre, 2003), which constitute the conflated unity of complex sounds. The prevalence among professional musicians differs between cultures: Prevalence rates in Japan have been reported up to 50% (P. K. Gregersen, Kowalsky, Kohn, & Marvin, 1999; Miyazaki, 1988), compared with estimates of 1–20% for professional Western musicians (Oliver Vitouch, 2003). It has been suggested that this effect in Japan is associated with the Suzuki method (P.K. Gregersen, Kowalsky, Kohn, & Marvin, 2001), a widespread pedagogical music approach in Japan, originally intended for violin training. The Suzuki music education emphasizes learning music by ear over reading musical notation and preferably begins with formal lessons early in life between the ages of 3 and 5 years.

1.2. Developmental aspects of absolute pitch

One fundamental reasoning in favor of the Suzuki method points to a parallelism between natural speech acquisition and purely auditory based musical training because the former also goes without any visual cues and is exclusively based on auditory feature learning (Kuhl, 2000). Hence, akin to language acquisition where a child learns to understand and to produce spoken language before learning to read, the Suzuki music education strives for acquisition of musical skills based on pure auditory sensation and production of music before learning to read music. Interestingly, memorization of musical pieces without referring to a notation is an important key issue of this approach, which particularly puts emphasis on auditory features, namely discrimination and representation of pitch and timbre. This makes children, who started musical training due to the Suzuki method early in their life, ideal candidates when it comes to studying the influence of auditory focused musical training on the development of the auditory system. Moreover, it has been shown that

the influence of an acquired tonal language like Mandarin can have a considerable impact on the development of AP: The prevalence of AP was far greater among the Chinese than the US students for each age level of musical training onset (Deutsch, Henthorn, Marvin, & Xu, 2006). Thus these authors suggested that a tonal language enables infants to associate pitches with verbal labels during the critical period in which features of their native language are acquired. And very recent study (Lee & Lee, 2010) showed impressively that 72% of Mandarin speaking professional musicians meet the criterion of having AP, whereas the performance level was negatively correlated with the onset of musical training – in other words: even if speaking tone language represents an advantage regarding AP performance, the onset of musical training seems to provide a robust impact on the development of extraordinary acuity of pitch naming ability.

1.3. Absolute pitch – result of nature or nurture?

Whether the extraordinary ability of AP is genetically determined or develops under the influence of environmental factors has attracted much debate (Levitin & Zatorre, 2003; Oliver Vitouch, 2003; Zatorre, 2003). Irrespective of the much-disputed role of the former (Athos et al., 2007; Drayna, 2007; Hove, Sutherland, & Krumhansl, 2010), there is considerable evidence for the substantial impact of early musical training on the development of AP (Baharloo, Johnston, Service, Gitschier, & Freimer, 1998; Miyazaki & Ogawa, 2006; Russo, Windell, & Cuddy, 2003). Presently there is a broad consensus that automatic language acquisition more likely yields native-speaker proficiency when it occurs before a critical age (Johnson & Newport, 1989; Kuhl, 2000; Lenneberg, 1967; Newport, 1990; Sakai, 2005). On the other hand, with respect to the development of AP, various studies suggest, that the acquisition of AP is strongly related to early musical exposure before the age of 6–7 (Baharloo et al., 1998; Baharloo, Service, Risch, Gitschier, & Freimer, 2000; Costa-Giomi, Gilmour, Siddell, & Lefebvre, 2001; P.K. Gregersen et al., 2001).

1.4. The role of absolute pitch in cognitive neurosciences

The extent to which language acquisition and AP ability develop in parallel suggests that AP ability might be regarded as a model of cortical plasticity for deliberate practice and musicianship. Thus it is assumed that the proficiency of musicians with AP should result in pertinent characteristics of auditory related cortical areas. Consistent with this notion are various structural observations of morphological changes in the cortical region of the planum temporale (PT) in musicians with AP (Keenan, Thangaraj, Halpern, & Schlaug, 2001; Luders, Gaser, Jäncke, & Schlaug, 2004; Schlaug, Jäncke, Huang, & Steinmetz, 1995; Wilson, Lusher, Wan, Dudgeon, & Reutens, 2009) and Heschl's gyrus (P. Schneider et al., 2005) in musicians with relative pitch (RP). These studies show that AP and professional musicianship in general leads to marked cortical gray matter alterations, mainly in the form of left-hemispheric asymmetries in speech-relevant areas. The pivotal role of the PT in auditory processing has been supported by a review article, in which the PT is taken to be a computational hub that is involved in processing different types of complex acoustic signals like environmental sounds, speech and music (Griffiths & Warren, 2002). Functional studies to date have revealed hemodynamic and electrophysiological lateralization effects in musicians with AP during processing of musical stimuli (Gaab, Schulze, Ozdemir, & Schlaug, 2006; Hirata, Kuriki, & Pantev, 1999; Ohnishi et al., 2001; P. Schneider et al., 2005; Wu, Kirk, Hamm, & Lim, 2008).

1.5. Musical expertise and language processing

By comparing nonmusicians and musicians with RP, several electrophysiological studies demonstrated a higher level of pitch decoding performance in language as a function of musical expertise (Itoh, Suwazono, Arao, Miyazaki, & Nakada, 2005; Magne, Schoen, & Besson, 2006; Carlos Marques, Moreno, Mazzucchi, Parma, & Cattelani, 1981; Schön, Magne, & Besson, 2004). There are however different levels of musical expertise, including superior AP, the functional importance of which is still unclear for speech processing. Because basic auditory processing is crucial for both speech and music perception, the relationship between musical expertise and speech processing needs to be examined. Prosodic variations, that is natural pitch modulations in spoken sentences, share many acoustic features with tone transitions

in musical melodies, which are mostly characterized as slow temporal variations of spectral units that span over several segments (Martin Meyer, Alter, Friederici, Lohmann, & von Cramon, 2002). The processing of delexicalized speech, effectively pure speech prosody, leads bilaterally to a significantly reduced neural activity of the posterior superior temporal gyrus (STG), PT and the planum polare (M. Meyer, Alter, & Friederici, 2003; Martin Meyer, Steinhauer, Alter, Friederici, & von Cramon, 2004). Besides these slow temporal variations - taken to be suprasegmental information in the presented stimuli - there are also fast temporal changes, signaling important information in speech and music: rapid spectro-temporal signal changes constitute the segmental information of speech (Hickok & Poeppel, 2007; Shannon, Zeng, Kamath, Wygonski, & Ekelid, 1995). In particular, important phonemic cues are indicated by these rapid signal changes. Without the ability to perceive them, one would probably be unable to discriminate, for example, between the words peer and beer. Precise phonetic processing and full dynamic lexical access therefore more efficiently contribute to a comprehensive semantic understanding (Poeppel, Idsardi, & van Wassenhove, 2008).

1.6. The superior longitudinal fasciculus (SLF)

The second study introduced in this thesis is focusing on anatomical characteristics of a particular fiber system, namely the superior longitudinal fiber tract (SLF), in AP and non-AP musicians (also called relative pitch possessors: RP). The SLF is of particular interest because it connects the temporal areas involved in lower and higher order auditory processing with frontal brain areas involved in the control of several executive functions (including working memory, attention and many more)(Geschwind, 1970; Hagmann, Cammoun et al., 2006). Evidently, the coordinated interplay between temporal and frontal brain areas is important for language and music functions (Aboitiz & Garcia, 1997, 2009; Friederici, 2009; Glasser & Rilling, 2008; Rilling et al., 2008; Vigneau et al., 2006). Thus it has been hypothesized that the evolution of this fiber tract is pivotal for the control of many cognitive functions, which are typical for human beings (e.g., language).

The SLF can be characterized as a bundle of white matter tracts including three distinct pathways: firstly, an anterior indirect segment connecting parietal cortical

fields (inferior parietal lobe) with the frontal lobe (frontal operculum); second, a posterior indirect segment, which connects the perisylvian (posterior superior temporal gyrus), the middle and inferior temporal region with the parietal lobe; and, third, a long direct segment connecting the temporal lobe with the frontal lobe (Catani & Mesulam, 2008). In addition, the large bundle of fibers connecting the posterior part of the temporoparietal junction with the frontal lobe, called arcuate fasciculus (AF), includes sections of the two frontal projecting SLF pathways. Thus, the AF is considered to be part of the SLF. To date, several studies, each pursuing a different strategy of diffusion tensor imaging (DTI) data and fiber tractography (FT) analysis, have succeeded in tracing and separating SLF pathways (Barrick, Lawes, Mackay, & Clark, 2007; Catani et al., 2007; Frey, Campbell, Pike, & Petrides, 2008; Makris et al., 2005; Makris et al., 2009; Upadhyay et al., 2008).

1.7. Training-induced plasticity in white matter structures

Diffusion tensor imaging (DTI) is the current standard for in-vivo study of white matter anatomy of the human or animal brain and has attracted increasing attention over the past decade. While standard imaging-based neuropsychological research focuses on function and anatomy of grey matter using functional magnetic resonance imaging (fMRI) or voxel-based morphometry (VBM), the in-vivo neuroimaging technique of DTI combined with fiber tracking (FT) offers a complementary way of exploring the architecture of white matter and axonal connectivity. DTI is based on magnetic resonance (MR) technology and provides measures of water diffusion in different spatial directions in the brain (Hagmann, Jonasson et al., 2006; Mori & Zhang, 2006). The most commonly studied diffusion parameter is fractional anisotropy (FA), which quantifies the directionality of diffusion within a voxel between 0 (undirected, isotropic) and 1 (directed, anisotropic and is derived from the diffusion tensor (Hagmann, Jonasson et al., 2006; Mori & Zhang, 2006).

FA has been found to increase during white matter maturation in the developing brain (Beaulieu, 2002; Cascio, Gerig, & Piven, 2007; Eluvathingal, Hasan, Kramer, Fletcher, & Ewing-Cobbs, 2007) and to decrease in the elderly (Bhagat & Beaulieu, 2004; Moseley, 2002). Reduced FA values have been reported in patients suffering from neurodegenerative diseases (Sundgren et al., 2004) or spinal cord injury

(Wrigley et al., 2008). Furthermore, FA has been found to be positively correlated with behavioural measures such as reading ability (Beaulieu et al., 2005; Klingberg et al., 2000; Niogi & McCandliss, 2006), performance in a speeded lexical decision task (Gold, Powell, Xuan, Jiang, & Hardy, 2007), and musical sensorimotor practice (Bengtsson et al., 2005). However the relations between white matter development, degeneration and training-induced plastic changes on the one hand and water diffusion characteristics on the other still remain poorly understood and a matter of controversy (Alexander, Lee, Lazar, & Field, 2007; Ashtari et al., 2007; Beaulieu, 2002). Notably only a small number of studies have tried to investigate the relationship between musical expertise, language associated cortical regions and related white matter structures using the DTI method, although it lends itself well to visualising characteristic aspects of white matter plasticity as a function of musical practice and extensive hearing experience: So far differences have been characterized by greater values of fractional anisotropy (FA) in the genu of the corpus callosum, lower FA in the corona radiata and the bilateral internal capsule, respectively (Schmithorst & Wilke, 2002). Another study, particularly focusing on the corticospinal tract (CST), confirmed significantly lower FA values in both hemispheres of musicians compared to non-musicians, whereas diffusivity in the CST was negatively correlated with the onset of musical training in childhood (Imfeld, Oechslin, Meyer, Loenneker, & Jäncke, 2009). Additionally, one DTI study identified positive correlations between the magnitude of local FA values and practice time in childhood and later life of professional musicians: bilaterally in the internal capsule, both in the splenium and the isthmus of the corpus callosum and in the ventral pathway of the right superior longitudinal fasciculus (SLF) (Bengtsson et al., 2005).

The above-mentioned studies confirmed white matter structure-function correspondence related to long-term musical training. Recent studies using fMRI and electroencephalography (EEG) provide strong evidence for alterations not only in music but also in speech processing modulated by musical expertise (Catani & Mesulam, 2008; C. Marques, Moreno, Castro, & Besson, 2007; Musacchia, Sams, Skoe, & Kraus, 2007; Oechslin, Meyer, & Jäncke, 2009; Schön et al., 2004). In this context, it would therefore be promising to focus on the white matter structure, which is responsible for a proper neural information supply in order to guarantee an accurate decoding of acoustic signals and speech production, respectively.

Several studies have shown that AP is related to processes and anatomical grey matter differences, which are lateralized to the left perisylvian brain area (Ohnishi et al., 2001; Schlaug, Jancke, Huang, & Steinmetz, 1995). The present study aimed to elucidate the extent to which white matter differences of the SLF reflect functional and anatomical lateralization effects in association with the acuity of AP.

2. Methods

2.1. Participants

Both introduced studies have been carried out with the same samples of subjects: Fifteen professional musicians with AP (8 females/7 males; mean age = 24 years, SD = 4.2; mean practice years = 18.4, SD = 2.9; mean age of practice begin = 5.7, SD = 2,2), fifteen professional musicians with RP (8 females/7 males, mean age = 25.3 years, SD = 2.8; mean practice years = 16.6, SD = 3.8; mean age of practice begin = 8.7, SD = 3) and fifteen NM without any musical expertise (NM: 8 females/7 males, mean age = 25.7, SD = 5.4) participated in this study. NM were selected on the basis that they had no musical practice for at least fifteen years. None of the subjects reported any hearing impairments. Due to some scanning artifacts while recording the white matter structure, only 13 subjects were taken for the analysis of the DTI data introduced in the second publications (see manuscripts for any further details).

2.2. Absolute pitch test

AP has been evaluated among all participating professional musicians with an in-house test that has been constructed by myself during an internship in the year 2005 at the Institute for Neuropsychology, University of Zurich: participants heard 108 pure sine wave tones, presented in pseudo-randomized order, which ranged from A3 (tuning: A4 = 440 Hz) to A5, while each tone was presented 3-fold. The accuracy was evaluated by counting correct answers - the semitone errors were taken as incorrect to increase the discriminatory power. Furthermore, the participants were not asked to identify the adjacent octaves of the presented tones, as for AP it is a most notable prerequisite to identify the correct chroma. Accurate detection of octaves is quite a difficult task, which is hardly possible even for musicians with AP.

Each tone of the AP test had duration of 1 s; the interstimulus interval (ISI) of 4 s was filled with brown noise. Subjects had to write down the tonal label immediately after they heard the accordant tone (i.e., while hearing the 4 s of brown noise). The whole test unit and its components were created with Adobe Audition 1.5.

2.3. General remarks on the experimental procedure and neuroimaging methods

The introduced studies use two different methodical approaches to observe functional and structural plasticity as a function of musical expertise. Both methods – functional magnetic resonance imaging (fMRI), and diffusion tensor imaging (DTI) - are described in detail in according methods sections of the two publications. Since DTI is a relatively new imaging method, however gets to date on a quite established level, the second publication provides a full methodical review, and besides a very detailed description of the DTI method itself.

Detailed information on the experimental procedure applied while recording fMRI can be found in the manuscript of the first introduced study on page 3.

3. Published original research articles

3. 1. Absolute Pitch – functional evidence of speech-relevant auditory acuity

Full citation:

Mathias S. Oechslin, Martin Meyer & Lutz Jäncke, *Absolute Pitch—Functional Evidence of Speech-Relevant Auditory Acuity*, Cerebral Cortex (2010), 20(2): 447-455. First published online 2009 July 10, doi: 10.1093/cercor/bhp113.

3.1.1. Abstract

Absolute pitch (AP) has been shown to be associated with morphological changes and neurophysiological adaptations in the planum temporale, a cortical area involved in higher-order auditory and speech perception processes. The direct link between speech processing and AP has hitherto not been addressed. We provide first evidence that AP compared with relative pitch (RP) ability is associated with significantly different hemodynamic responses to complex speech sounds. By systematically varying the lexical and/or prosodic information of speech stimuli, we demonstrated consistent activation differences in AP musicians compared with RP musicians and nonmusicians (NM). These differences relate to stronger activations in the posterior part of the middle temporal gyrus and weaker activations in the anterior mid-part of the superior temporal gyrus. Furthermore, this pattern is considerably modulated by the auditory acuity of AP. Our results suggest that the neural underpinnings of pitch processing expertise exercise a strong influence on propositional speech perception (sentence meaning).

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Absolute Pitch—Functional Evidence of Speech-Relevant Auditory Acuity

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Absolute pitch (AP) has been shown to be associated with morphological changes and neurophysiological adaptations in the planum temporale, a cortical area involved in higher-order auditory and speech perception processes. The direct link between speech processing and AP has hitherto not been addressed. We provide first evidence that AP compared with relative pitch (RP) ability is associated with significantly different hemodynamic responses to complex speech sounds. By systematically varying the lexical and/or prosodic information of speech stimuli, we demonstrated consistent activation differences in AP musicians compared with RP musicians and nonmusicians. These differences relate to stronger activations in the posterior part of the middle temporal gyrus and weaker activations in the anterior mid-part of the superior temporal gyrus. Furthermore, this pattern is considerably modulated by the auditory acuity of AP. Our results suggest that the neural underpinnings of pitch processing expertise exercise a strong influence on propositional speech perception (sentence meaning).

Keywords: absolute pitch, fMRI, musical expertise, speech processing

Introduction

"Absolute pitch" (AP) is a very rare phenomenon among professional musicians, enabling them to identify tones without the aid of any reference tone. In terms of cognitive music psychology, AP could be characterized as the ability to distinguish and identify one salient quality (the pitch chroma) from a number of other perceptual attributes (Levitin and Zatorre 2003), which constitute the conflated unity of complex sounds. The prevalence among professional musicians differs between cultures: Prevalence rates in Japan have been reported up to 50% (Miyazaki 1988; Gregersen et al. 1999) compared with estimates of 1–20% for professional Western musicians (Vitouch 2003). It has been suggested that this effect is associated with the Suzuki method (Gregersen et al. 2001), which is a widespread pedagogical music approach in Japan originally intended for violin training The Suzuki music education emphasizes learning music by ear over reading musical notation and preferably begins with formal lessons early in life between the ages of 3 and 5 years. One fundamental reasoning in favor of this education points to a parallelism between natural speech acquisition and purely auditory based musical training because the former also goes without any visual cues and is exclusively based on auditory feature learning (Kuhl 2003). Hence, akin to language acquisition where a child learns to understand and to produce spoken language before learning to read the Suzuki music education strives for acquisition of musical skills based on pure auditory sensation and production of music before learning to read music. Interestingly, memorization of musical pieces without referring to a notation is an important key issue of this approach which particularly puts emphasis on auditory features, namely discrimination and representation of pitch and timbre. This makes children who started musical training due to the Suzuki method early in their life ideal candidates when it comes to studying the influence of auditory focused musical training on the development of the auditory system. Moreover, it has been shown that the influence of an acquired tonal language like Mandarin can have a considerable impact on the development of AP: The prevalence of AP was far greater among the Chinese than the US students for each age level of musical training onset (Deutsch et al. 2006). Thus these authors suggested that a tonal language enables infants to associate pitches with verbal labels during the critical period in which features of their native language are acquired.

Whether the extraordinary ability of AP is genetically determined or develops under the influence of environmental factors has attracted much debate (Vitouch 2003; Zatorre 2003; Levitin and Rogers 2005). Irrespective of the much disputed role of the former (Athos et al. 2007; Drayna 2007), there is considerable evidence for the substantial impact of early musical training on the development of AP (Baharloo et al. 1998; Russo et al. 2003; Miyazaki and Ogawa 2006). Presently there is a broad consensus that automatic language acquisition more likely yields a native-speaker proficiency when it occurs before a critical age (Lenneberg 1967; Johnson and Newport 1989; Newport 1990; Kuhl 2000; Sakai 2005). On the other hand, with respect to the development of AP, various studies suggest, that the acquisition of AP is strongly related to early musical exposure before the age of 6–7 (Baharloo et al. 1998, 2000; Costa-Giomi et al. 2001; Gregersen et al. 2001). The extent to which language acquisition and AP ability develop in parallel suggests that AP ability might be regarded as a model of cortical plasticity for deliberate practice and musicianship. Thus it is assumed that the proficiency of musicians with AP should result in pertinent characteristics of auditory related cortical areas. Consistent with this notion are various structural observations of morphological changes in the cortical region of the planum temporale (PT) in musicians with AP (Schlaug et al. 1995; Keenan et al. 2001; Luders et al. 2004; Wilson et al. 2008) and Heschl's gyrus (Schneider et al. 2005) in musicians with relative pitch (RP). These studies show that AP and professional musicianship in general leads to marked cortical gray matter alterations, mainly in the form of left-hemispheric asymmetries in speech-relevant areas. The pivotal role of the PT in auditory processing has been supported by a review article, in which the PT is taken to be a *computational hub* (Griffiths and Warren 2002) that is involved in processing different types of complex

acoustic signals like environmental sounds, speech and music. Functional studies to date have revealed hemodynamic and electrophysiological lateralization effects in musicians with AP during processing of musical stimuli (Hirata et al. 1999; Ohnishi et al. 2001; Schneider et al. 2005; Gaab et al. 2006; Wu et al. 2008). By comparing nonmusicians and musicians with RP, several electrophysiological studies demonstrated a higher level of pitch decoding performance in language as a function of musical expertise (Marques et al. 1981; Schön et al. 2004; Itoh et al. 2005; Magne et al. 2006). There are however different levels of musical expertise, including superior AP, the functional importance of which is still unclear for speech processing. Because basic auditory processing is crucial for both speech and music perception, the relationship between musical expertise and speech processing needs to be examined. Prosodic variations, that is natural pitch modulations in spoken sentences, share many acoustic features with tone transitions in musical melodies, which are mostly characterized as slow temporal variations of spectral units that span over several segments (Meyer et al. 2002). The processing of delexicalized speech, effectively pure speech prosody, leads bilaterally to a significantly reduced neural activity of the posterior superior temporal gyrus (STG), PT and the planum polare (Meyer et al. 2003, 2004). Besides these slow temporal variations—taken to be *suprasegmental* information in the presented stimuli—there are also fast temporal changes, signaling important information in speech and music: rapid spectrotemporal signal changes constitute the *segmental* information of speech (Shannon et al. 1995; Hickok and Poeppel 2007). In particular, important phonemic cues are indicated by these rapid signal changes. Without the ability to perceive them one would probably be unable to discriminate, for example, between the words *peer* and *beer*. Precise phonetic processing and full dynamic lexical access therefore more efficiently contribute to a comprehensive semantic understanding (Poeppel et al. 2008).

Regarding the neural basis of language comprehension, a linguistically based model of spoken language comprehension discriminates between *segmental* and *suprasegmental* information of speech (Friederici and Alter 2004). Particularly in terms of the *dynamic dual pathway model* the authors argue, that *segmental* information (phonemes, syntactic and lexial–semantic elements) are primarily processed in a left hemisphere temporo-frontal pathway whereas *suprasegmental* information (sentence level prosody) is processed in a right hemispheric temporo-frontal pathway. Moreover, the authors imply dynamic interactions between the hemispheres, due to a disentangling of prosodic and semantic information during auditory sentence comprehension. With respect to the neural processing of *segmental* speech, it has been shown (Meyer et al. 2004) that the left hemisphere STG and superior temporal sulcus (STS) activations are most strongly driven by *segmental* information processing irrespective of whether the presented speech stimuli comprise prosodic pitch variations (that is *suprasegmental* information) or not. This finding goes in line with the *dual stream model* proposed by Hickok and Poeppel (2007). Their *dual stream model of cortical organization of speech processing* assumes a *dorsal stream*, which is mainly involved in speech production, connecting left-hemispheric posterior supratemporal regions with inferior frontal areas. Complementarily they claim a *ventral stream*, which in principle is bilaterally represented. The *ventral stream* is thought to be responsible for a mediation of spectrotemporal (STG) and phonological (STS) analyses with lexical units located in inferior temporal regions. Moreover, a proposed lexical interface (middle temporal gyrus [MTG], inferior temporal sulcus) subserves these processes by gating and collating basic auditory and lexical memory information.

This proposed link between basal auditory and higher-order speech information processing leads to the main hypothesis of this paper assuming a link between musical expertise (especially for AP musicians) and higher-order (lexical and/or prosodic) speech information processing.

A recently published diffusion tensor imaging study (Glasser and Rilling 2008) focused on 2 distinct seeding regions (STG and STS/MTG) in the left hemisphere in order to track the superior longitudinal fasciculus (SLF)—the main pathway in association with speech perception and production. The authors overlaid activation findings from other studies using either lexical, phonemic or prosodic language stimuli. They showed that activations based on lexical speech stimuli corresponded to the MTG seeding region of interest (ROI), whereas phonemic processing was associated with the STG seeding ROI. Thus, the authors demonstrated a left lateralized functional association of lexical speech processing by taking into account the morphological architecture of the SLF. Furthermore, we have been able to demonstrate that local alterations of diffusion parameters among the SLF are associated with key regions (like MTG and inferior frontal gyrus [IFG]) by means of higher-order language processing, and modulated by different levels of musical expertise (Oechslin et al. forthcoming).

Applying brain imaging methods musicians with AP have not been studied so far with respect to speech processing. To date all imaging studies published have used musical stimuli during functional MRI. Exemplary Ohnishi and colleagues (Ohnishi et al. 2001) observed enhanced responses in the left PT while AP musicians listened to melodies, whereas other studies have shown that the right auditory cortex is preferentially activated when nonmusicians process music (Tervaniemi et al. 2001; Janata et al. 2002; Overy et al. 2004).

Based on these findings showing enhanced responses in the left PT and adjacently located perisylvian brain regions in AP musicians to musical stimuli we assume that there is an increased proficiency of AP individuals also in language processing. In particular, we posit a left-sided lateralization also in language comprehension as a function of musical expertise irrespective of linguistic domain (syntax, semantics, phonology).

This idea is supported by several studies which reported anatomical and functional alterations in left-sided perisylvian brain areas of AP musicians (Schlaug et al. 1995; Steinmetz 1996; Keenan et al. 2001; Luders et al. 2004; Wilson et al. 2008). It is also conceivable that AP musicians use their augmented pitch memory (Gaab et al. 2006) ability to more efficiently identify linguistically relevant pitch information than do RP and nonmusicians (NM). If this is indeed the case, AP musicians might show less activation in left-sided perisylvian brain areas when processing linguistic speech stimuli.

In order to elucidate the possible link between the acuity of AP and speech perception we designed the present functional magnetic resonance imaging (fMRI) experiment in which meaning and intonation in spoken language were systematically varied. We were specifically interested in whether AP musicians demonstrate different cortical activation patterns in

association with lexical as compared with prosodic speech information. Because AP musicians demonstrate particular morphological and functional alterations in the left PT region, we reasoned that left-sided perisylvian and adjacent extrasylvian areas (STS, MTG) would be differently involved in higher-order speech processing. Therefore, we anticipated that these differences would occur within the ventral pathway as delineated by Hickok and Poeppel (Hickok and Poeppel 2007).

Materials and Methods

Subjects and AP Test

Fifteen professional musicians with AP (8 females/7 males; mean age = 24 years, SD = 4.2; mean practice years = 18.4, SD = 2.9; mean age of practice begin = 5.7, SD = 2,2), fifteen professional musicians with RP (8 females/7 males, mean age = 25.3 years, SD = 2.8; mean practice years = 16.6, SD = 3.8; mean age of practice begin = 8.7, SD = 3) and fifteen NM without any musical expertise (NM: 8 females/7 males, mean age = 25.7, SD = 5.4) participated in this study. NM were selected on the basis that they had no musical practice for at least fifteen years. None of the subjects reported any hearing impairments. All participants were tested for their handedness with the Annett Handedness Inventory (Annett 1967). All of them had normal structural scans and did not suffer from any neurological disorders. We evaluated AP among all participating professional musicians with an in-house test: participants heard 108 pure sine wave tones, presented in pseudorandomized order, which ranged from A3 (tuning: A4 = 440 Hz) to A5, while each tone was presented 3-fold. The accuracy was evaluated by counting correct answers—the semitone errors were taken as incorrect to increase the discriminatory power. Furthermore, the participants were not asked to identify the adjacent octaves of the presented tones, as for AP it is a most notable prerequisite to identify the correct chroma. Accurate detection of octaves is quite a difficult task, which is hardly possible even for musicians with AP.

Each tone of the AP test had a duration of 1 s; the interstimulus interval (ISI) of 4 s was filled with brown noise. Subjects had to write down the tonal label immediately after they heard the accordant tone (i.e., while hearing the 4 s of brown noise). The whole test unit and its components were created with Adobe Audition 1.5. The AP test was performed with a Dell Laptop Latitude 300x and presented via Sennheiser HD-25-1 headphones.

The Experimental Procedure

The 4 conditions (Fig. 1), which encompass the manipulation of spoken German phrases are characterized as follows: *normal speech* (yielding proper propositional speech), *delexicalized speech* (representing pure speech melody/prosody or pitch contour), *flattened speech* (representing pure lexical and syntax information—comprising sentence meaning and lacking dynamic pitch contour) and *flattened-delexicalized speech* (combined application of the prior 2 manipulations, lacking both sentence meaning and dynamic pitch contour). Delexicalizement of speech signals leads to a masking of lexical and syntactic information as a result of the PURR-filtering procedure (Sonntag and Portele 1998). This kind of manipulation produces speech stimuli containing only prosodic speech parameters such as intonation, duration, amplitude envelope and the second and third formants. The procedure to generate *flattened speech* is based on a readjustment of the pitch contour F_0, in which all natural pitch variations are kept constant on the level of 200 Hz. All stimuli were normalized on the same moderate amplitude level. These 4 conditions are conceived as the expression of 2 dimensions representing prominent speech inherent characteristics, namely *segmental* and *suprasegmental* information. *Delexicalized speech* and *flattened speech* represent the first and the second dimension of our experimental design and are each defined by 2 levels (*suprasegmental* on/off and *segmental* on/off). The third dimension is defined by *expertise*—the between-subject variable—which determines 3 levels of musical expertise: AP, RP, and musically untrained subjects. Given this experimental design our fMRI data analysis was performed by means of a 3-way ANOVA with repeated measurements (*segmental* × *suprasegmental* × *expertise*). This ANOVA reveals

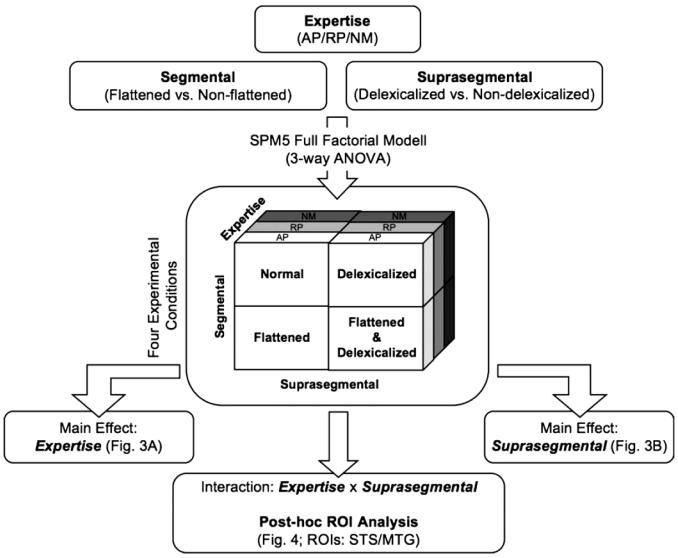

Figure 1. In this figure the methodical framework is depicted. The 3 factors *expertise*, *suprasegmental* and *segmental* leads us to an orthogonal design that has been calculated by using a full factorial design (3-way ANOVA), provided by SPM5: *expertise* (AP/RP/NM) × *segmental* (flattened vs. nonflattened) × *suprasegmental* (delexicalized vs. nondelexicalized). The significant interaction *expertise* × *suprasegmental* has been further analyzed by applying a post hoc ROI analysis comparing delexicalized versus nondelexicalized conditions.

cortical activation clusters that represent significant main effects and interactions respectively. To assure the participants' attention, all subjects were instructed to judge whether a sentence contains suprasegmental information (i.e., prosody) or not, and to respond via a response box after each trial. Each condition comprised 40 sentences. Stimuli of the 4 conditions being presented in pseudorandomized order, evenly distributed in 4 separate runs (each 10.6 min). Each sentence had a duration of about 5 s followed by an ISI of 11 s, resulting in a trial length of 16 s—an adequate time window to model the blood oxygenation level-dependent (BOLD) response. The sentences started in a jittered order to preserve the variance within the BOLD signal (onset-times for sentences: 1, 500, 1000, 1500, 2000 ms).

Data Acquisition and Analysis

During the scanning session the participants were instructed to keep their eyes open and to focus a fixation cross. Binaural auditory stimulation was presented by a digital playback system including a high frequency shielded transducer system. This acoustic transmission system includes a piezoelectric loudspeaker enabling the transmission of strong sound pressure levels (105 dB) with excellent attenuation characteristics (Jäncke et al. 2001). T_2^*-weighted echo planar imaging (EPI) was acquired on a 3.0 tesla GE magnet resonance scanner (imaging parameters: echo time = 32 ms, repetition time = 2 sec, flip-angle = 70 deg., FOV = 22 cm, slice thickness = 3.4 mm, voxel size = 3.4 mm × 3.4 mm, slices per volume = 32, volumes = 302). The data analysis was performed with the parametric mapping software SPM5 (http://www.fil.ion.ucl.ac.uk/spm/). The preprocessing consisted of spatial realignment, normalization to a standard EPI template and a smoothing procedure with a 6-mm Gaussian kernel. Due to the experimental design, the analysis was proceeded in an event-related manner; therefore the standardized canonical HRF was applied to model the BOLD response. For further group level analysis we specified the SPM5 factorial design built up by 3 independent variables resulting in a 2 × 2 × 3 ANOVA: *segmental* (2 levels: un-/flattened sentences), *suprasegmental* (2 levels: un-/delexicalized sentences) and *expertise* (3 levels: AP/RP/NM). The reported main effects and interactions are all proceeded on the $P < 0.001$ level (unc.) with an extended cluster threshold of $k = 5$ voxels. Furthermore, to elucidate hemispheric asymmetries during speech processing as a function of musical expertise we performed a post hoc ROI-analysis regarding the interaction *segmental* × *expertise*. The software *marsbar* (http://marsbar.sourceforge.net/) was used to define 7-mm sphere ROIs bilaterally at maximal local *F*-values reflecting the 2 predefined left-hemispheric clusters (Fig. 4*A*: ROI 1, STS, [−54, −37, 6]; ROI 2, MTG, [−51, −39, −6]). Mean BETA values were read out by in-house programmed MATLAB (http://www.mathworks.com/) scripts and further analyzed by a general linear model with repeated measures and *t*-tests (SPSS, http://www.spss.com/).

Results

Forty-five healthy volunteers participated in our study. They were grouped according to 3 distinctive levels of musical expertise: AP possessors, RP possessors, and nonmusicians (NM) without any musical expertise as controls. The professional musicians (AP/RP) performed an in-house designed AP test. Using a behavioral AP performance index (Fig. 2, AP test score), 2 distinct experimental groups were formed. The data show a clear distinction between the 2 groups, whereas AP accuracy is heterogeneously distributed within the groups (AP: $n = 15$, mean = 82.2%, SD = 16.2; RP: $n = 15$, mean = 6.9%, SD = 4.2). Due to the conservative scoring technique used in this experiment, the performance data indicate that most of the AP musicians have high AP ability. However, the subjects' scores speak against an all-or-none dichotomy regarding the special phenomenon of AP.

To maintain motivation during the fMRI task procedure, subjects were asked to pay attention to the prosodic aspect of the spoken German sentences and to judge each stimulus as to whether it contained prosody or not. Subjects heard 4 different types of acoustic stimuli which were distinguishable along the 2 independent dimensions of *segmental* and *suprasegmental* speech information. Furthermore, the third dimension is defined as *expertise*, enabling (Fig. 1) a 3-way ANOVA (for further specifications see *the experimental procedure* in the methods section). The prosody detection task was not selective and resulted in a ceiling level of accuracy, irrespective of condition and experimental group.

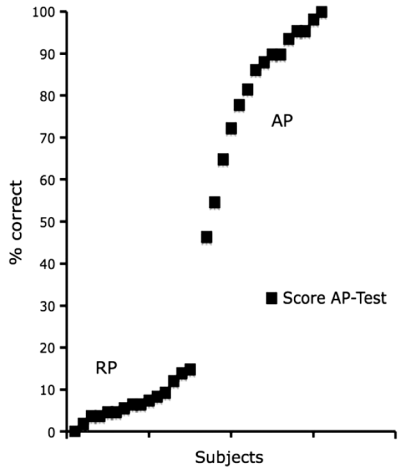

Figure 2. Plotted scores of the AP test (AP [$n = 15$, Average: 82.2%, SD: 16.2] and RP [$n = 15$, Avg.: 6.9%, SD: 4.2]).

All significant clusters representing main effects and interactions based on the performed SPM5 full factorial design (3-way ANOVA) are listed in Table 1. The main effect *expertise* (Fig. 3*A*) is characterized by a bilateral activation of the STG (STG-right; [63, −12, 3], F = 11.79; STG-left; [−57, −9, 3], $F = 11.32$), with the peak of the main effect in the right hemisphere STG. The plotted mean BETA values (Fig. 3*A*) show exactly the same activation pattern in the comparison of the 3 groups over the 4 conditions, the activation in the right STG cluster is considerably enhanced compared with the left STG cluster. This main effect was observed in each condition, the weakest activations were found in musicians with AP.

The significant main effect *suprasegmental* (Fig. 3*B*) reflects predominately left-hemispheric activation in perisylvian regions that constitute the core language network, namely the STS, MTG, IFG, and the inferior temporal gyrus (ITG). The robust main effect *suprasegmental* (activation peak at the left MTG; [−57, −45, 0], $F = 88.89$) can be explained by systematically enhanced brain responses to meaningful sentences. In other words, when comparing the conditions comprising lexical information (*normal* and *flat*) with the conditions lacking lexical information (*delexicalized* and *flattened-delexicalized*), much larger BOLD signals were elicited in the former condition, and here again with a stable distribution across the levels of musical expertise.

The observation of an interaction between lexical information processing and expertise deserves particular consideration: The significant interactions *suprasegmental* × *expertise*

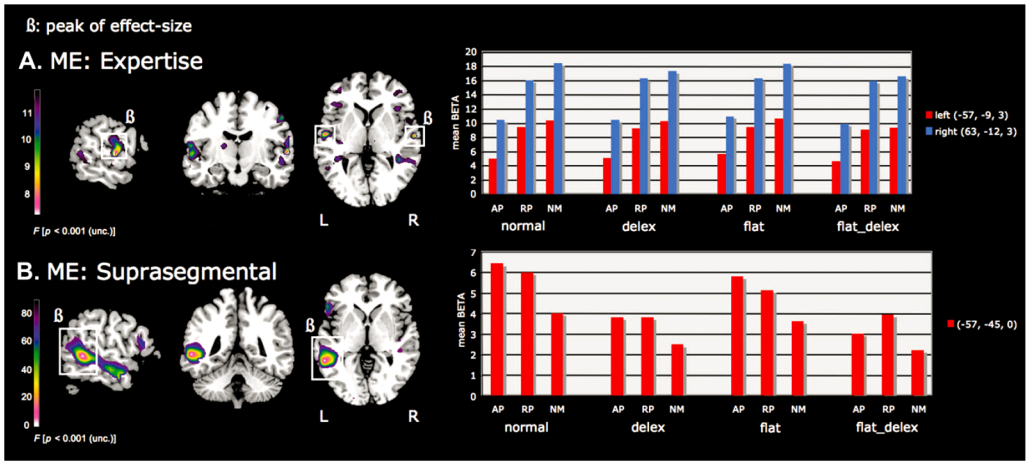

Figure 3. Selected results of the 3-way ANOVA (*segmental* × *suprasegmental* × *expertise*) On the left side, cortical views show the significant results of a full factorial design performed with SPM5: (*A*) the main effect *expertise* (STG, PT) and (*B*) the main effect *suprasegmental* (MTG, STG, ITG). On the right, mean BETA values at the sites of effect peaks (white small boxes) are plotted for all 3 groups of subjects (AP/RP/NM) and against the 4 experimental conditions: *normal speech* (normal), *delexicalized speech* (delex), *flattened speech* (flat) and *flattened-delexicalized speech* (flat_delex).

uncovered a left temporal cluster which is located on the transition strip between the lower bank of the posterior STS and the superior bank of the MTG [(−54, −37, 6), $F = 9.28$]—as this cluster is located considerably inside the sulcus we henceforth use the term STS. Additionally we found a more anterior located cluster on the MTG [(−51, −39, −6), $F = 9.28$]; both clusters are characterized by the same effect size of interaction (Fig. 4*A*). The precise anatomical location was evaluated by applying the *Harvard-Oxford cortical structural atlas* (available at: http://www.cma.mgh.harvard.edu/) and the *Destrieux-Atlas* (Fischl et al. 2004), which has been implemented in *FreeSurfer* software (available at: http://surfer.nmr.mgh.harvard.edu/).

We also conducted a ROI-analysis to more closely examine the relationship between musical expertise and segmental information processing (Figs 1, 4).

First, we defined 2 ROIs based on the interaction peaks of the 2 clusters (Fig. 4*A*: ROI 1, STS, [−54, −37, 6]; ROI 2, MTG, [−51, −39, −6]).

Secondly, we created 2 sphere-ROIs (Bosch 2000) to investigate lateralization effects (Fig. 4*B*).

And thirdly, we conducted four 2-way ANOVAs (*hemisphere* × *expertise*) with repeated measurements based on the mean BETA values for each ROI under each processing condition, that is, nondelexicalized processing (collapsed data of *normal speech* and *flattened speech*) and delexicalized processing (collapsed data of *delexicalized speech* and *flattened-delexicalized speech*) (Fig. 1).

The ANOVA revealed for ROI 1 a main effect for *hemisphere* in the delexicalized conditions ($F_{1,42} = 43.6$, $P < 0.001$); the analysis of ROI 1 obtained in the nondelexicalized conditions revealed a significant main effect for *hemisphere* ($F_{1,42} = 67.2$, $P < 0.001$) and an interaction *hemisphere* × *expertise* ($F_{2,42} = 4.3$, $P < 0.05$). The BETA values for ROI 2 revealed a main effect for *expertise* both in the delexicalized conditions ($F_{2,42} = 3.4$, $P < 0.05$) and in the nondelexicalized conditions ($F_{2,42} = 4.3$, $P < 0.05$). In order to further specify the interaction effects, post hoc tests were conducted (corrected for multiple comparisons) (Fig. 4*C*). The main effect *segmental* did not reveal any suprathreshold cluster ($P < 0.001$ [unc.]).

These findings can be summarized as follows: The main effect *hemisphere* is explained by a strongly left-sided lateralization of activation in the STS. The *hemisphere* × *expertise* interaction relies on the fact that the AP group shows significantly stronger activity in the left than in the right hemisphere during the presentation of segmental speech information. Thus, the STS should be considered an area that supports higher auditory function in AP possessors. However, it should be mentioned that we did not find any interhemispheric difference in the MTG. There was also a main effect for *expertise* in the MTG as shown with post hoc tests revealing higher mean BETA values in musicians than in nonmusicians, whereas there were no significant interhemispheric activation differences. Interestingly, the AP group did not differ in the MTG from the RP group of the musicians. However, the AP musicians showed a highly significant activity enhancement in the left-hemispheric MTG when comparing nondelexicalized with delexicalized categories of stimulus manipulations (Fig. 4*D*).

Discussion

Based on recent studies (Schön et al. 2004; Magne et al. 2006; Wong et al. 2007) one might expect an enhanced sensitivity for pitch contours in musicians during prosodic processing. However, the present study did not reveal a significant main effect when prosody is manipulated (Table 1: main effect [ME] segmental). Notably, as the methodological approaches (event related potentials, brainstem-potentials) and tasks in aforementioned studies clearly differ from our design it is difficult to compare the results, last but not least due to temporal constraints associated with fMRI and the BOLD signal. Unlike the previously mentioned electroencephalography (EEG) studies, the fMRI

Table 1
Significantly activated brain regions broken down for the main effects (ME) and interactions (INT)

Regions	Voxels	F	Coordinates LH			Coordinates RH		
			x	*y*	*z*	*x*	*y*	*z*
ME expertise								
STG/PT	14	11.79	—	—	—	63	−12	3
STG/PT	18	11.32	−57	−9	3	—	—	—
RO		8	−60	−9	12	—	—	—
MTG	19	10.89	—	—	—	54	−42	−3
MTG (subgyral)		9.16	—	—	—	42	−42	0
PCG	9	9.58	—	—	—	54	−9	48
ME suprasegmental								
MTG	745	88.89***	−57	−45	0	—	—	—
MTG		61.77***	−54	−15	−15	—	—	—
ITG		56.15***	−57	−6	−24	—	—	—
MTG		54.77***	−51	6	24			
STG		26.24***	−51	−51	18			
IFG	194	46.43***	−54	24	3	—	—	—
IFG		38.91***	−51	18	15	—	—	—
ITG	77	46.14***	—	—	—	57	−9	−21
IFG	32	45.4***	−48	27	−9	—	—	—
SFG	34	28.61**	−9	57	33	—	—	—
SFG		16.7	−12	60	24	—	—	—
PRE	93	20.73	−9	−75	39	—	—	—
PRE		17.83	−18	−66	24	—	—	—
mdFG	39	19.08	−6	39	30	—	—	—
mdFG		14.02	—	—	—	6	39	27
AG	29	18.49	−51	−60	39	—	—	—
PRE	51	17.2	—	—	—	18	−63	21
C		15.4	—	—	—	15	−72	36
IPS	20	15.93	−39	−54	51	—	—	—
MTG	25	14.98	—	—	—	48	−33	−6
mdFG	5	12.35	−3	6	18	—	—	—
ME segmental								
No suprathreshold voxels								
INT suprasegmental × expertise								
MTG	8	9.28	−51	−39	−6	—	—	—
STS	10	9.28	−54	−57	6	—	—	—

Note: This table reports all significant clusters revealed by the SPM full factorial design ($k = 5$, $P < 0.001$ [unc.]), what corresponds to a 3-way ANOVA (*Expertise* × *Segmental* × *Suprasegmental*) Main effects (ME) of *Expertise*, *Suprasegmental*, *Segmental*, and the interaction (INT) *Expertise* × *Suprasegmental* are specified by anatomical labels, cluster size (voxels), the local peak effects (*F* value), and the coordinates of the local peak in the left (LH) and right (RH) hemisphere, respectively. Astersiks ([***] $P < 0.001$, [**] $P < 0.01$) indicate significant clusters due to correction for multiple tests (FWE). PCG, postcentral gyrus; RO, rolandic operculum; IPS, intraparietal sulcus; SFG, superior frontal gyrus; PRE, precuneus; mdFG, medial frontal gyrus; AG, angular gyrus; C, Cuneus.

technique focuses on quite different time frames due to coarser resolution during cortical speech processing. Given the results of these studies, the question may be raised whether AP musicians show an exceptional sensitivity for prosodic processing—however, AP should be considered a phenomenon that differs from standard musical proficiency (which is the subject of investigation in the above cited studies) and may not imply an enhanced sensitivity to prosodic information.

In our statistical analysis the main effect of *expertise* is characterized by bilateral activation on the superior temporal plane with a slight right-hemispheric preponderance (Fig. 2*A*). Musical expertise, irrespective of whether the presented stimuli contained prosodic/lexical information does not account for this finding. The activation pattern is characterized as follows: the higher the musical training—in particular with respect to AP—the lower the activation in the specific region of primary auditory information processing. Accordingly, musical expertise is the main driving factor explaining different activations in the core auditory regions, thus extending recent findings of other research groups (Schneider et al. 2002; Wong et al. 2008).

The main effect of *expertise* possibly indicates more efficient processing by the auditory cortex as a function of musical proficiency. Using EEG, positron emission tomography, and fMRI, the principles of neural efficiency have been discussed within several different contexts such as spatial perception (Vitouch et al. 1997), superior cognitive performance by figural intelligence in chess players (Grabner et al. 2006) and working memory (Grabner et al. 2004). The data provided by these studies imply that higher performance levels are associated with lower cortical activations. Additionally, this relationship has been found (Haier et al. 1992) even as a consequence of "Tetris" learning effects, which were associated with a decrease of local glucose metabolic rates. In general, these authors propose that "brighter" (or more proficient) subjects have to invest less cortical resources to achieve accurate performances. Conversely, cognitively less proficient subjects had to invest more cortical resources to solve the same tasks. From an anatomical point of view, it has been demonstrated, that more gray matter in distinct cortical regions (primary auditory cortex and PT amongst others) is associated with higher IQs; more gray matter also results in less use of energy, when the area is engaged (efficiently) in specific cognitive tasks (Haier et al. 2004).

This argumentation is in line with studies focusing on sensory information processing in the visual cortex (Marcar et al. 2004a). The *standard model* put forward by these authors holds that an increase in the electrical activity and an increase in size of the activated neural population have an opposing influence on the BOLD signal amplitude (Marcar and Loenneker 2004). In a nutshell, this model states that the vascular response is controlled by electrical discharge activity, whereas the oxygen consumption is dependent on the size of the activated neuronal population. Based on an experimental MR setting different checkerboard patterns were presented (flashed vs. reversing), whereas the size of activated neural populations has been manipulated (Marcar et al. 2004b). The results demonstrated that the checkerboard which is associated with a lower neural activity yielded a larger number of activated voxels and a stronger BOLD response.

These results are contradictory to the *Linear Transfer Model* which states that the BOLD contrast signal is directly proportional to the neuronal activity.

In the context of language comprehension, it has been demonstrated that the neural correlates of semantic priming support the neural efficiency hypothesis (Rissman et al. 2003): Semantically related word pairs showed consistently less activation than unrelated pairs—interestingly, with respect to the temporal lobe this activation pattern is restricted to the left STG, and does not affect the MTG. As the authors argue, the perception of a prime word activates a lexical–semantic network that shares common elements with the target word, and, thus, the target can be recognized with enhanced neural efficiency. The proposed relationship between STG and MTG is striking, because the MTG—which doubtlessly is crucial for lexical–semantic processes—does not contribute to the pattern of neural efficiency, drawn by the recruitment of the neural population, which is responsible for primary auditory signal decoding.

Furthermore, in interpreting the main effect of *expertise*, which is characterized by lowest activation of the STG bilaterally in AP and highest activations in NM, it might be useful to recall the characteristic morphological lateralization of Heschl's Gyrus (Schneider et al. 2005) in professional musicians and the PT in professional musicians with AP

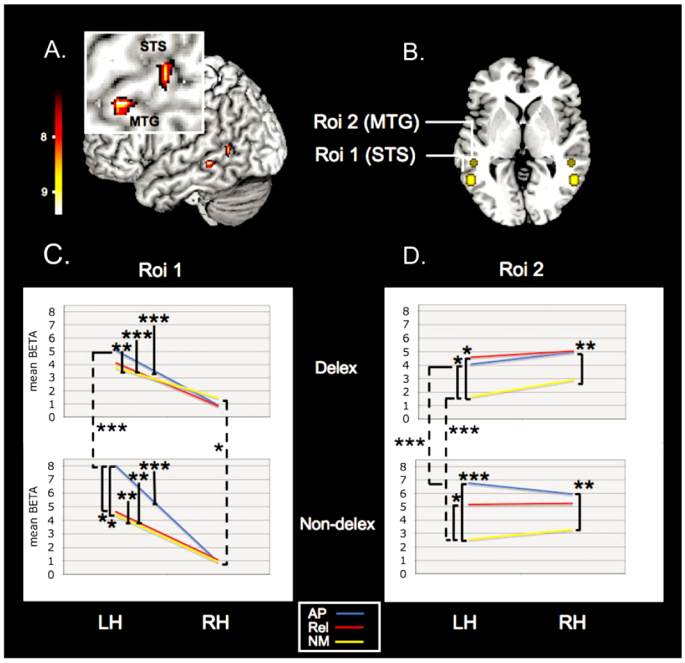

Figure 4. Detailed data of ROI-analysis regarding the significant interaction *suprasegmental* × *expertise* (*A*) STS and MTG interaction cluster with two equivalent left-hemispheric peaks of interaction (ROI 1 [STS]: (−54, −57, 6), $F = 9.28$; ROI 2 (MTG): (−51, −39, −6), $F = 9.28$, $P < 0.001$, $k = 5$), (*B*) two post hoc defined ROIs according to the peaks of interaction at left STS and MTG (left hemisphere) and two corresponding mirror related ROIs (right hemisphere). The left two (C) and right two (D) plots are defined by the separately assigned two clusters of significant interaction (ROI 1: [−54, −57, 6], $F = 9.28$; ROI 2: [−51, −39, −6]). The upper two plots represent the mean BETA values for the collapsed delexicalized conditions (*delexicalized speech* and *flattened-delexicalized speech*) in the left (LH) and the right (RH) hemisphere respectively, and the lower two plots represent the mean BETA values for the collapsed nondelexicalized conditions (*normal speech* and *flattened speech*); asterisks indicate significant levels (*$P <$ 0.05, **$P < 0.01$, ***$P < 0.001$) as revealed by un-/paired *t*-tests.

(Schlaug et al. 1995; Keenan et al. 2001). Due to an increased size of these structures in the left hemisphere, it seems reasonable to assume that they subserve auditory processing by means of an optimal contribution, characterized by the above-discussed neural efficiency hypothesis. Thus, the revealed main effect of *expertise* can be taken to be the first evidence for neural efficiency in basal auditory processing of language as a function of musical expertise.

When considering the main-effect *suprasegmental*, left temporal brain areas comprising posterior parts of the STG, STS, MTG, and ITG are more strongly activated during processing of lexical and propositional information (Fig. 3*B*). Consistent with this is the finding that the posterior MTG and the lower bank of the posterior STS are involved in lexical and phonetic analyses (Binder et al. 2000; Dick et al. 2007). Essentially, many authors of clinical and nonclinical studies have maintained that the left MTG plays a specific role in lexical and semantic processing (Binder et al. 2000; Dick et al. 2007). By applying *voxel-based lesion-symptom mapping* it has been shown that the posterior MTG is one of the main areas involved in higher-order language processing (Bates et al. 2003; Dronkers et al. 2004). In addition, functional neuroimaging studies support the special role of the posterior MTG in language processing. At least one study that investigated word ambiguity (Rodd et al. 2005) showed elegantly the involvement of the posterior MTG in semantic analyses. Accordingly, there should be a strong link between the auditory cortex and the posterior MTG during lexical information processing. Therefore, both the auditory cortex and the MTG are essential for a proper distinguishing between the words *beer* and *peer*. With respect to this we found a strong interaction between the factors *suprasegmental* and *expertise* located in the left MTG, which is characterized by stronger responses to lexical compared with delexicalized information, with musicians showing the strongest difference. With respect to the main effect *expertise* this activation pattern does not conflict with the above-discussed efficiency hypothesis. As already mentioned, due to the cortical recruitment of lexical-semantic networks it has been demonstrated that primary auditory processing is driven by the principles of neural efficiency, whereas the activity of the MTG shows a different activation pattern which cannot be explained using this line of argumentation. Nevertheless, the MTG provides core evidence for lexical-semantic processing (Rissman et al. 2003).

In general, these results are also in line with the *dual stream model* (Hickok and Poeppel 2007) that postulates a lexical interface located in the posterior part of the left MTG (part of

the *ventral stream*). Contrary to strong left-sided activations of the posterior STS due to segmental speech processing (Friederici and Alter 2004), activations of the posterior MTG are specific to musicianship, with musicians (with AP or RP) demonstrating stronger bilateral hemodynamic responses compared with nonmusicians. According to the 2-way ANOVAs (motivated by the findings due to the *expertise* × *suprasegmental* interaction, see Fig. 1), the main effect *expertise* in both delexicalized and nondelexicalized conditions lets us suggest that the MTG might be crucial for higher-level language processing. The post hoc tests show a significant enhancement of effect sizes in this area in musicians compared with nonmusicians (Fig. 4*C*). In addition, the analysis of posterior STS (Fig. 4*C*) revealed that AP musicians show stronger left lateralized activations during processing of segmental information compared with the other 2 groups. This finding is in line with several reports of left-sided enhanced levels of activation in AP musicians during complex auditory tasks (Pantev et al. 1998; Ohnishi et al. 2001; Itoh et al. 2005). Based on these findings, we propose that the auditory acuity of AP is not limited to basal auditory processing (usually conceived in terms of music processing), but extends to a more general notion of acoustic segmentation by fully integrating left-hemispheric speech-relevant networks.

Taken together, our study presents 2 novel findings: First, there is an AP-specific enhancement of the left lateralized activation in the lower bank of the posterior STS for segmental speech processing; second, musicians generally demonstrate stronger bilateral BOLD effects in the posterior MTG in all conditions. In addition, this effect of segmental processing is substantially enhanced in AP musicians compared with the other 2 experimental groups. This novel insight lets us conclude that neurofunctional alterations due to musicianship are not only manifested in exceptional acuity of music processing, but also affect speech processing in the sense that AP represents a comprehensive analytical proficiency for acoustic signal decoding.

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3.2.1. Abstract

Previous neuroimaging studies have demonstrated that musical expertise leads to functional alterations in language processing. We utilized diffusion tensor imaging (DTI) to investigate white matter plasticity in musicians with absolute pitch (AP), relative pitch and non-musicians. Using DTI, we analyzed the fractional anisotropy (FA) of the superior longitudinal fasciculus (SLF), which is considered the most primary pathway for processing and production of speech and music. In association with different levels of musical expertise, we found that AP is characterized by a greater left than right asymmetry of FA in core fibers of the SLF. A voxel-based analysis revealed three clusters within the left hemisphere SLF that showed significant positive correlations with error rates only for AP-musicians in an AP-test, but not for musicians without AP. We therefore conclude that the SLF architecture in AP musicians is related to AP acuity. In order to reconcile our observations with general aspects of development of fiber bundles, we introduce the Pioneer Axon Thesis, a theoretical approach to formalize axonal arrangements of major white matter pathways.

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The plasticity of the superior longitudinal fasciculus as a function of musical expertise: a diffusion tensor imaging study

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Previous neuroimaging studies have demonstrated that musical expertise leads to functional alterations in language processing. We utilized diffusion tensor imaging (DTI) to investigate white matter plasticity in musicians with absolute pitch (AP), relative pitch and non-musicians. Using DTI, we analysed the fractional anisotropy (FA) of the superior longitudinal fasciculus (SLF), which is considered the most primary pathway for processing and production of speech and music. In association with different levels of musical expertise, we found that AP is characterized by a greater left than right asymmetry of FA in core fibres of the SLF. A voxel-based analysis revealed three clusters within the left hemisphere SLF that showed significant positive correlations with error rates only for AP-musicians in an AP-test, but not for musicians without AP. We therefore conclude that the SLF architecture in AP musicians is related to AP acuity. In order to reconcile our observations with general aspects of development of fibre bundles, we introduce the Pioneer Axon Thesis, a theoretical approach to formalize axonal arrangements of major white matter pathways.

Keywords: DTI, absolute pitch, plasticity, musical expertise, superior longitudinal fasciculus, white matter, language, pioneer axon thesis

INTRODUCTION

The musician's brain has attracted much attention in recent years of neuroscience research as a model for brain plasticity (Münte et al., 2002). This research has shown that musicians demonstrate specific anatomical features related to their specific training expertise. In particular, those brain areas involved in controlling music-specific behaviour (auditory perception, motor control, and memory processes) reveal anatomical differences compared with non-musicians (NM). For example, there are differences between musicians and NM in volume and grey matter density in the auditory cortex, including Heschl's gyrus and the planum temporale (Schlaug et al., 1995a; Keenan et al., 2001; Schneider et al., 2002, 2005, 2009; Lüders et al., 2004; Hänggi et al., 2008; Bermudez et al., 2009). In addition to the auditory cortex, there are differences in Broca's area, the motor cortex, the cerebellum and parts of the parietal cortex (amongst others) between musicians and NM (Elbert et al., 1995; Schlaug et al., 1995b; Sluming et al., 2002, 2007; Gaser and Schlaug, 2003; Hutchinson et al., 2003; Bangert et al., 2006).

Besides these anatomical differences, numerous studies have shown that musicians process auditory and motor information differently, as indicated by neurophysiological measures (Pantev et al., 1998; Jäncke et al., 2000, 2006; Münte et al., 2002; Lotze et al., 2003; Fujioka et al., 2004, 2005; Peretz and Zatorre, 2005; Shahin et al., 2005; Koeneke et al., 2006; Baumann et al., 2007, 2008; Lappe et al., 2008; Herholz et al., 2009; Oechslin et al., 2010). Most of these studies have attributed these effects to the daily hours of intensive training over many years. Since most of these studies are cross-sectional in nature it is difficult to attribute these differences directly to music practice. However, some studies directly support the idea of practice-dependent effects in musicians. For example, Pantev and colleagues have shown that training can be instrument-specific (Pantev et al., 2001; Schulz et al., 2003; Shahin et al., 2008), and that the electroencephalography (EEG) responses of children taking music lessons change differently over the course of a year compared with those of children not studying music (Fujioka et al., 2006). A further finding is that musicians who have improved their auditory functions show also improved language functions as well as more efficient processing of language (Besson et al., 2007; Marques et al., 2007; Imfeld et al., 2009; Moreno et al., 2009; Oechslin et al., 2010).

In this study, we focus on a specific subgroup of musicians, namely those with absolute pitch (AP). In general, AP is defined as the ability to detect a pitch without any tonal reference. But it is still a matter of debate whether the extraordinary hearing acuity of AP develops due to musical training or is genetically determined (Vitouch, 2003; Levitin and Rogers, 2005). Regarding the neural underpinnings of AP, it has been shown that AP is characterized by specific features, mostly related to anatomical and physiological features and the specific role of the left hemisphere and left-sided perisylvian brain areas in particular. For example, a left-hemispheric volumetric asymmetry in the planum temporale (Schlaug et al., 1995a; Keenan et al., 2001; Gaser and Schlaug, 2003) has been reported. In terms of cortical activations, various studies demonstrated hemodynamic and electrophysiological lateralization effects (mostly favouring the left hemisphere) in musicians with AP while processing both music (Ohnishi et al., 2001; Schön et al., 2004; Gaab et al., 2006) and speech stimuli (Oechslin et al., 2010).

In the present study, we explored the anatomical characteristics of a particular fibre system, namely the superior longitudinal fibre tract (SLF), in AP and non-AP musicians [also called relative

pitch (RP) possessors]. The SLF of particular interest because it connects the temporal areas involved in lower and higher order auditory processing with frontal brain areas involved in the control of several executive functions (including working memory, attention and many more) (Geschwind, 1970; Hagmann et al., 2006a). Evidently, the coordinated interplay between temporal and frontal brain areas is important for language and music functions (Aboitiz and Garcia, 1997, 2009; Glasser and Rilling, 2008; Rilling et al., 2008; Friederici, 2009). Thus it has been hypothesized that the evolution of this fibre tract is pivotal for the control of many cognitive functions, which are typical for human beings (e.g. language).

The SLF can be characterized as a bundle of white matter tracts including three distinct pathways: firstly, an anterior indirect segment connecting parietal cortical fields (inferior parietal lobe) with the frontal lobe (frontal operculum); second, a posterior indirect segment, which connects the perisylvian [posterior superior temporal gyrus (STG)], the middle and inferior temporal region with the parietal lobe; and, third, a long direct segment connecting the temporal lobe with the frontal lobe (Catani and Mesulam, 2008). In addition, the large bundle of fibres connecting the posterior part of the temporoparietal junction with the frontal lobe, called arcuate fasciculus (AF), includes sections of the two frontal projecting SLF pathways. Thus, the AF is considered to be part of the SLF. To date, several studies, each pursuing a different strategy of diffusion tensor imaging (DTI) data and fibre tractography (FT) analysis, have succeeded in tracing and separating SLF pathways (Makris et al., 2005, 2009; Barrick et al., 2007; Catani et al., 2007; Frey et al., 2008; Upadhyay et al., 2008).

DTI is the current standard for *in vivo* study of white matter anatomy of the human or animal brain and has attracted increasing attention over the past decade. While standard imaging-based neuropsychological research focuses on function and anatomy of grey matter using functional magnetic resonance imaging (fMRI) or voxel-based morphometry (VBM), the *in vivo* neuroimaging technique of DTI combined with fibre tracking (FT) offers a complementary way of exploring the architecture of white matter and axonal connectivity. DTI is based on magnetic resonance (MR) technology and provides measures of water diffusion in different spatial directions in the brain (Hagmann et al., 2006b; Mori and Zhang, 2006). The most commonly studied diffusion parameter is fractional anisotropy (FA), which quantifies the directionality of diffusion within a voxel between 0 (undirected, isotropic) and 1 (directed, anisotropic and is derived from the diffusion tensor (Hagmann et al., 2006b; Mori and Zhang, 2006). Since white matter in the brain consists of aligned axonal fibres, diffusion is constrained perpendicular to the orientation of these fibre bundles, which leads to anisotropic diffusion. The principal direction of diffusion reflects the orientation of a fibre bundle in a specific voxel and is, therefore, exploited by fibre tracking algorithms. The mean diffusivity (the trace of the diffusion tensor) is a measure for the amount of diffusion, which can be divided into an axial diffusivity component ($\lambda_{||}$, diffusion along the axons) and a radial diffusivity component ($\lambda_{\perp}$, diffusivity perpendicular to the axons). While $\lambda_{||}$ corresponds to the first eigenvalue of the diffusion tensor ($\lambda_{||} = \lambda_1$), $\lambda_{\perp}$ is calculated by averaging the second and third eigenvalue: $\lambda_{\perp} = (\lambda_2 + \lambda_3)/2$ (Alexander et al., 2007).

FA has been found to increase during white matter maturation in the developing brain (Beaulieu, 2002; Cascio et al., 2007; Eluvathingal et al., 2007) and to decrease in the elderly (Moseley, 2002; Bhagat and Beaulieu, 2004). Reduced FA values have been reported in patients suffering from neurodegenerative diseases (Sundgren et al., 2004) or spinal cord injury (Wrigley et al., 2009). Furthermore, FA has been found to be positively correlated with behavioural measures such as reading ability (Klingberg et al., 2000; Beaulieu et al., 2005; Niogi and McCandliss, 2006), performance in a speeded lexical decision task (Gold et al., 2007), and musical sensorimotor practice (Bengtsson et al., 2005). However the relations between white matter development, degeneration and training-induced plastic changes on the one hand and water diffusion characteristics on the other still remain poorly understood and a matter of controversy (Beaulieu, 2002; Alexander et al., 2007; Ashtari et al., 2007). Notably only a small number of studies have tried to investigate the relationship between musical expertise, language associated cortical regions and related white matter structures using the DTI method, although it lends itself well to visualizing characteristic aspects of white matter plasticity as a function of musical practice and extensive hearing experience: So far differences have been characterized by greater values of FA in the genu of the corpus callosum, lower FA in the corona radiata and the bilateral internal capsule, respectively (Schmithorst and Wilke, 2002). Another study, particularly focusing on the corticospinal tract (CST), confirmed significantly lower FA values in both hemispheres of musicians compared to NM, whereas diffusivity in the CST was negatively correlated with the onset of musical training in childhood (Imfeld et al., 2009). Additionally, one DTI study identified positive correlations between the magnitude of local FA values and practice time in childhood and later life of professional musicians: bilaterally in the internal capsule, both in the splenium and the isthmus of the corpus callosum and in the ventral pathway of the right SLF (Bengtsson et al., 2005).

The above-mentioned studies confirmed white matter structure–function correspondence related to long-term musical training. Recent studies using fMRI and EEG provide strong evidence for alterations not only in music but also in speech processing modulated by musical expertise (Schön et al., 2004; Marques et al., 2007; Musacchia et al., 2007; Catani and Mesulam, 2008; Oechslin et al., 2010). In this context, it would therefore be promising to focus on the white matter structure, which is responsible for a proper neural information supply in order to guarantee an accurate decoding of acoustic signals and speech production, respectively.

Several studies have shown that AP is related to processes and anatomical grey matter differences, which are lateralized to the left perisylvian brain area (Schlaug et al., 1995b; Ohnishi et al., 2001). The present study aimed to elucidate the extent to which white matter differences of the SLF reflect functional and anatomical lateralization effects in association with the acuity of AP.

MATERIALS AND METHODS

PARTICIPANTS AND ABSOLUTE PITCH TEST

A total number of 39 subjects participated in this study: 13 professional musicians with AP, 13 professional musicians with RP, and 13 NM as control subjects. All musicians had started musical practice before the age of 10 (**Table 1**). All participants were

Table 1 | This table displays group specific data of gender, age, practice start, total amount of practice years and errors in the AP-test (mean ± SD). None of the parameters differs significantly with respect to the observed experimental groups except the evaluated AP performance [one-tailed *t*-test for independent samples: $p < 0.001$ ($t = 18.75$), Kolmogorov–Smirnov test demonstrated normally distributed AP-test performance in RPs and APs ($p > 0.2$)].

	Gender (m/f)	Age	Practice start	Amount of practice years	Errors AP-test
Musicians with absolute pitch (AP)	5/8	24.6 ± 3.3	6 ± 1.8	18.6 ± 2.4	16.2 ± 14.9
Musicians with relative pitch (RP)	5/8	24.6 ± 2.1	7.5 ± 2.1	17.1 ± 3.2	98.9 ± 5.6
Non-musicians (NM)	6/7	25.6 ± 5.3	–	–	–

tested for their hand preference using the Annett Handedness Questionnaire (Annett, 1967) and were verified according to the procedure described by Annett as consistent right-handers. The musicians played a variety of instruments including the violin, viola, piano, trombone and the traverse flute. Local ethical committee approval was obtained and all subjects provided written informed consent consistent with the Declaration of Helsinki.

We evaluated AP among professional musicians (AP and RP) with an in-house designed test: participants heard 108 pure sine wave tones, presented in pseudo-randomized order, which ranged from A3 (tuning: A4 = 440 Hz) to A5, while each tone was presented ninefold (threefold in each octave). The accuracy was evaluated by counting correct answers – the semi-tone errors were taken as incorrect to increase the discriminatory power by means of AP. Furthermore, the participants were not asked to identify the adjacent octaves of the presented tones, as for AP it is a most notable prerequisite to identify the correct chroma. Accurate detection of octaves is quite a difficult task, which is hardly possible even for musicians with AP.

Each tone of the AP-test had duration of 1 s; the inter-stimulus interval (ISI) of 4 s was filled with brown noise. Subjects had to write down the tonal label immediately after they heard the accordant tone (i.e. while hearing the 4 s of brown noise).

DTI DATA ACQUISITION

We performed DTI on a 3T whole body MR system (Signa Excite II, GE Healthcare, Milwaukee, USA) using a standard 8-channel head coil. Axial imaging was performed in accordance with an imaging plane parallel to the anterior–posterior commissural (AC–PC) line. We sampled the diffusion tensor by repeating a diffusion-weighted single-shot spin-echo echo-planar sequence along 21 different geometrical directions. Diffusion sensitization was achieved with two balanced diffusion gradients centred on the 180° radio-frequency pulse. An effective *b*-value of 1000 s/mm^2 was used for each of the 21 diffusion-encoding directions. Three measurements were performed without diffusion weighting (b_0 of 0 s/mm^2) at the beginning of the sequence. Scan parameters were TR = 8000 ms; TE = 91 ms; matrix size = 128 × 128; and FOV = 240 × 240 mm. A total of 42 contiguous 3-mm-thick axial sections were acquired. Data quality was examined using DTI-Studio (Jiang et al., 2006). And bad slices were excluded from analysis (11 bad slices out of all acquired slices (39 × 24 × 42 = 39312) in the three groups (AP/RP/NM) of participants).

PREPROCESSING

FA and mean diffusivity (trace) images were calculated in native space using DTI-Studio (Jiang et al., 2006). Preprocessing of these images consisted of four steps: (1) brain extraction, (2) nonlinear normalization to Montreal Neurological Institute (MNI) space, (3) smoothing for voxel-wise analysis, and (4) thresholding for selection of white matter only.

Normalization was done by estimating the morphing parameters from a nonlinear normalization of the mean b_0 image's grey matter component to SPM5's grey matter probability map. These parameters where then applied to the FA and diffusivity images, resulting in accurate alignment of the SLF in all subjects. The smoothing kernel of 8 mm was chosen according to standards in DTI literature (Snook et al., 2007). However, for ROI analysis we used unsmoothed data (voxel size 2 × 2 × 2 mm) to avoid partial volume contribution by signal from neighbouring non-white matter voxels. Thresholding for selection of white matter only was done by subjecting FA and diffusivity images to a combined threshold of FA >0.25 and trace <0.004.

FIBRE TRACTOGRAPHY

In order to determine regions for ROI analysis, SLF probability maps for each group and each hemisphere were created, using deterministic FT. First, diffusion tensors were calculated in MNI stereotaxic standard space for every subject using the diffusion II toolbox for *SPM* available at htttp://souceforge.net/projects/spmtools. The tensor data were transformed into a data format amenable to the DTI&Fibre Tools software package for fibre tracking and visualization (Kreher et al., 2006). Using this software, a deterministic fibre-tracking algorithm (Mori et al., 1999) was performed on the whole brain, initiating a fibre at the centre of every voxel. Tracking was automatically terminated if the FA value of the current voxel dropped below 0.15 or mean diffusivity exceeded 0.002, indicating grey matter or cerebro-spinal fluid voxels. Fibres were also terminated if the angle between the principal eigenvectors of the current and the next voxel exceeded 53.1° (Kreher et al., 2006).

According to the described fibre tracking strategy by Mori et al. (2002) a multi-ROI approach in MNI space was used to select the SLF fibre structure. As depicted in **Figure 1** we used two spatially separated ROIs to reconstruct the whole SLF pathway (Catani et al., 2007) – this procedure covers both the indirect (parietal-frontal-projection) and direct pathway (temporo-parieto-frontal projection).

Since fibre tracking was performed in MNI space, the process of extracting the individual fibre structures of each subject was automated in order to reduce observer bias. The resulting fibre structures were visually inspected and only an ignorable number of spurious fibres not belonging to the SLF had to be eliminated manually.

Visit masks (ROIs marking voxels which contain fibres of a specific fibre tract) were generated for the SLF fibre structure in the two hemispheres of every subject. These binary visit-masks

were averaged across subjects (13 subjects per group) in order to obtain group probability maps for each hemisphere as shown in **Figure 2**.

ROI ANALYSIS BASED ON THRESHOLDED SLF PROBABILITY MAPS

Group-specific ROIs for the left and the right SLF were derived from the probability maps by applying a threshold at $p < 0.05$, to obtain volumetric regions with a maximized probability of fibre trajectories. Thus we extracted volumetric ROIs of asymmetric shapes that represent group and hemisphere specific fibre volumes in voxels (**Figure 3**). This approach allows registration of subtle differences of SLF volumes between groups and hemispheres that would be washed out when using a standard approach. Extraction of binary ROIs from probability maps was used within *SPM5* (http://www.fil.ion.ucl.ac.uk/spm/software/spm5/). Mean FA-values were extracted from the ROIs of all 39 subjects using an in-house written Matlab script. Two-way ANOVA (hemisphere × expertise) with one repeated measurements factor (hemisphere) and subsequent two-tailed paired samples *t*-tests (Bonferroni corrected for multiple comparisons) and was performed to evaluate hemispheric differences as a function of musical expertise.

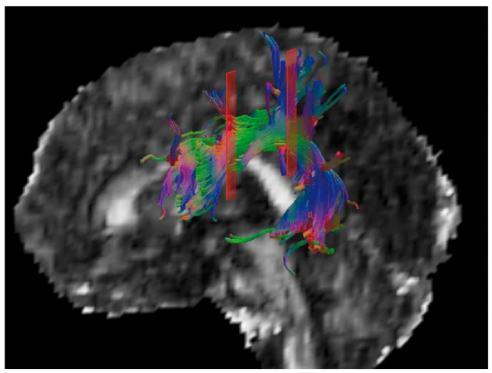

FIGURE 1 | A 3-D model of the left SLF of a single subject is displayed. The red areas indicate the anterior and posterior ROI used for creating the SLF fibre subset. Only fibres running through both ROIs are considered to be part of the tracked fibre structure.

VOXEL-WISE ANALYSIS OF MUSICIANS' SLF

To examine the relation between local anisotropic characteristics and AP-test performance, we performed multiple regression within *SPM5*. To focus on the SLF structure bilaterally this voxel-wise analysis, we used the AP group-specific unthresholded probability map as binary template for bilateral explicit masking (**Figure 4**). Subsequently, significant clusters [$p < 0.01$ (unc.), $k = 5$] were extracted using the *SPM5* toolbox *marsbar*, and served as ROIs for the analysis of individual FA maps. Although one might be dubious about the application of cluster ROIs instead of more established spherical ROIs, we prefer to apply the former in this case, since this strategy allows the most precise determination with respect to the SLF structure (defined by the SLF binary mask) and white matter in general. This procedure has been executed in both groups of musicians (AP and RP), but not in NM, since the latter group is not able to perform the AP-test due to musical illiteracy. Furthermore, we correlated mean FA values with the AP-test errors of the accordant group by calculating the Pearson's correlation coefficients (**Figure 5**).

RESULTS

The SLF delineated on the basis of the probability maps is shown in **Figure 3**. Based on six *a priori* defined ROIs (3 groups × 2 hemispheres) the mean FA values were subjected to a two-way ANOVA [*expertise* (AP/RP/NM) × *hemisphere* (LH/RH)] with repeated measurements on one factor (*hemisphere*) and revealed significantly between-hemisphere differences as a function of musical expertise [interaction *expertise* × *hemisphere*: $F(2,36) = 7.04, p < 0.01$]. In order to qualify this interaction we conducted subsequent *post-hoc* paired *t*-tests ($p < 0.05$, Bonferroni corrected) and identified that AP musicians showed a significant left-greater-than-right lateralization ($t = 2.8$, $p = 0.016$). NM on the other hand showed a significant right-greater-than-left lateralization ($t = -2.79$, $p = 0.016$), whereas RP showed no inter-hemispheric differences ($t = -0.63$, $p = 0.543$; **Table 2**).

Multiple regression of APs' FA maps using their AP-test error rates as covariates revealed three clusters located exclusively within the left-hemispheric SLF indicating significant positive correlations between error rates and FA indices of APs (**Figure 5A**). In other words, high performance in the AP-test is associated with low mean FA values within the observed regions. These clusters are situated in portions of the SLF which connect anterior, posterior and perisylvian regions that are essential for the cortical organization of speech processing (Hickok and Poeppel, 2007): The first one, representing the cluster with the highest correlation effect (−28, −28,

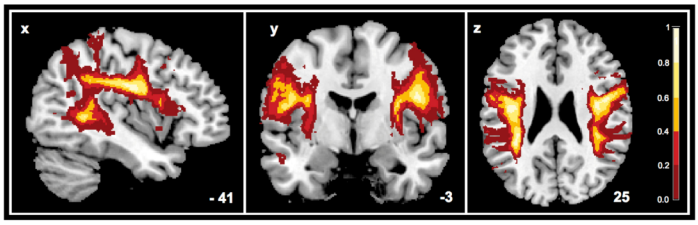

FIGURE 2 | Here the probability map for the SLF of the AP group (*n* = 13) is illustrated – combined for two hemispheres. Voxels are displayed with unthresholded probabilities.

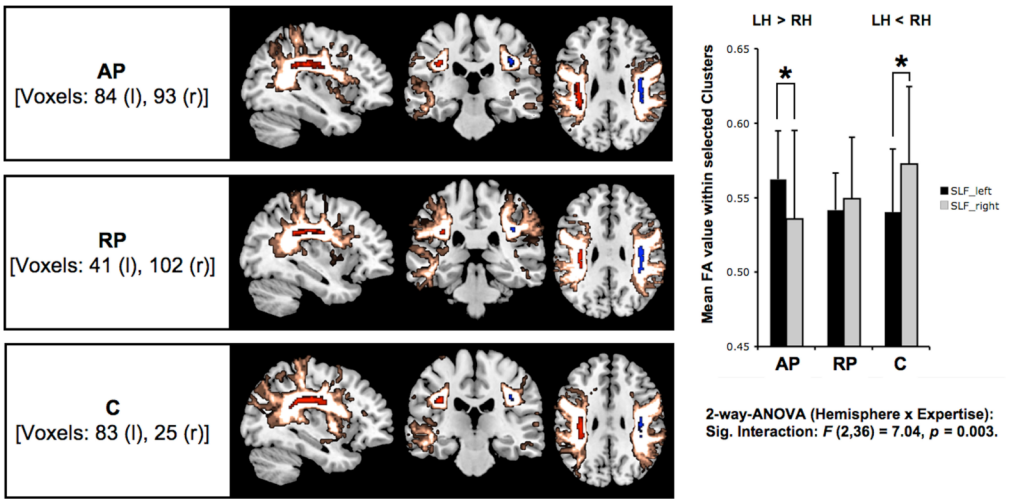

FIGURE 3 | The ROIs calculated by thresholding probability maps of bilateral SLFs' are illustrated in red (left) and blue (right), surrounded by unthresholded group specific probability maps (gold). The bar chart illustrates for each group and both hemispheres the standard deviation (error bars) and means of FA values calculated by comprising all suprathreshold voxels within the defined ROIs ($p < 0.05$). Asterisks indicate significant inter-hemispheric within-group differences (*$p < 0.05$) as a result of *t*-tests for paired samples (two-tailed). Moreover, the between-group analysis (two-way ANOVA) revealed a significant interaction *expertise* × *hemisphere*.

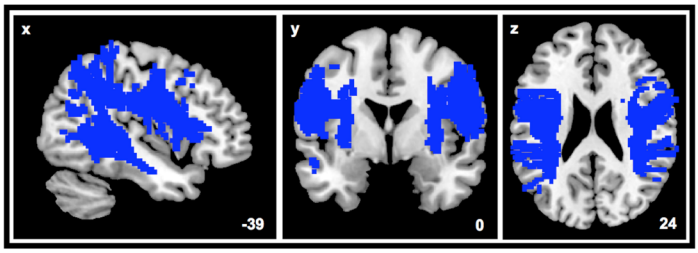

FIGURE 4 | The unthresholded probability map of the bilateral SLF served as template to create the illustrated binary mask while performing the voxel-wise analysis.

44; $k = 6$, $t = 4.15$, $p = 0.01$, uncorrected; **Figure 5B**) is located at the superior border of the frontoparietal SLF projection, next to the fundus of the postcentral gyrus; the second is located deeply within the inferior-frontal ramifications projecting into the frontal operculum (−40, −2, 22; $k = 9$, $t = 3.16$, $p = 0.01$, uncorrected; **Figure 5C**); and the third most extended cluster is located laterally at the SLF's posterior indirect segment projecting to the inferior temporal sulcus and the middle temporal gyrus (MTG) (−42, −50, 4; $k = 20$, $t = 3.94$, $p = 0.01$, uncorrected; **Figure 5D**).

Based on the ROI analysis, as described in Section "Materials and Methods," and the correlation of mean FA indices of the cluster ROIs with the AP's error rates, we emphasize the relationship indicated by voxel-wise analysis: In relation to the auditory acuity of AP, all clusters revealed significant ($p < 0.01$) positive correlations (r) between 0.69 and 0.77 ($n = 13$), whereas in RP there is no evidence for a relationship between their error rates and FA values for the same sample of ROIs (**Figure 5**).

DISCUSSION

This study focused on alterations in white matter as a function of musical training and exceptional hearing abilities. Our specific interest, as outlined in the introduction and reflected in our analysis, concerned whether and to what extent there are differences in FA-values within the SLF structure between (1) musicians and NM, and (2) between musicians with and without AP. Firstly, we discuss ROI-based effects of hemispheric lateralizations that reflect

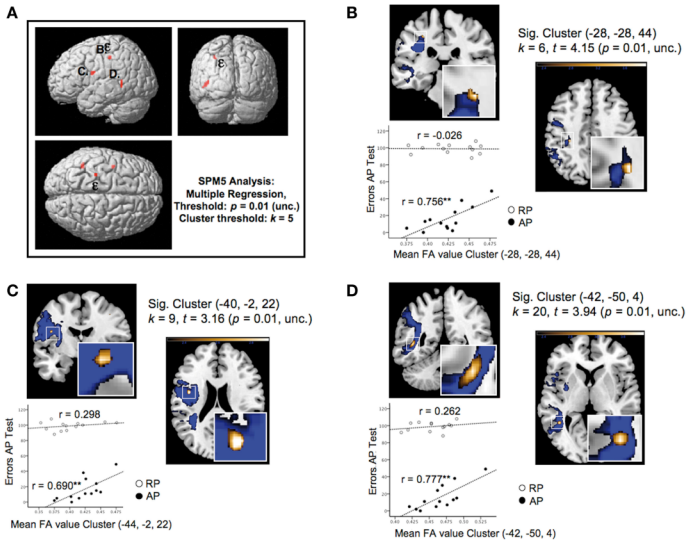

FIGURE 5 | (A) Shows the three significant clusters (B–D) identified by a voxel-wise multiple regression, characterized by FA values which significantly correlate with the error rates of the APs in the AP-test. The highest correlational effect [designated by the epsilon (ε)] has been identified as the most superior located cluster **(B)** of the SLF. **(B–D)** provides close inspections of the significant clusters and plotted correlations obtained by the additional ROI analysis, which is based on the identified clusters in APs (see Section "Materials and Methods"). Accordingly, the error rates are plotted against mean FA values of RP and AP found by the ROI analysis. Asterisks (**$p < 0.01$) indicate the level of significance with respect to the calculated correlational coefficients (Pearson's *r*). Furthermore, **(B–D)** provides additional information concerning the corresponding cluster [*k* = number of voxels, *t* = highest *t*-value within the cluster, (*x*, *y*, *z*) = coordinates of the peak voxel of each cluster in MNI space].

Table 2 | The upper part of this table contains the descriptive data (mean ± SD) reflecting the performed ROI analysis based on thresholded probability maps. Additionally, the t-tests (*p < 0.05) show within-group differences (Bonferroni corrected) of the mean FA values between the left (LH) and the right hemisphere (RH).

	AP	RP	NM
FA left SLF (mean ± SD)	0.562 ± 0.04	0.542 ± 0.05	0.540 ± 0.05
FA right SLF (mean ± SD)	0.536 ± 0.05	0.549 ± 0.03	0.573 ± 0.06
***t*-Tests (paired, two-tailed) LH vs. RH**			
t	2.8	–0.63	–2.79
p	0.016*	0.543 (n.s.)	0.016*

between-group differences. Secondly, our discussion emphasizes AP-specific FA characteristics for the SLF as a whole. Finally, we discuss our results in the context of myelination principles and axonal formation and we introduce the *Pioneer Axon Thesis*.

ROI ANALYSIS DUE TO PROBABILITY MAPS

The utilization of group-specific probability maps for ROI generation revealed a lateralization effect as a function of musical expertise (as revealed by the ANOVA). We found greater left than right lateralization of mean FA values in AP and greater right than left lateralization in NM, while there was no significant lateralization effect in RP. In contrast, the analysis of the complete structure of SLF, by averaging FA values of all corresponding voxels (**Figure 4**), revealed no significant lateralization effect as a function of musical expertise.

The group-specific lateralization of mean FA values (**Figure 3**) cannot be explained by differences in the biographic variables age, onset of musical training, or total amount of practice years (**Table 1**). The inclusion of these biographical parameters – both partial (corrected for age) and bivariate – in our correlational approach allows us to rule out any significant relationship between these demographic parameters[1] and mean FA values within the ROIs of the left/right hemisphere in all three groups. A meaningful influence of these factors on the demonstrated group-specific lateralization effects appears unlikely. The significant interaction *expertise* × *hemisphere* and the results of *post-hoc t*-tests suggest that the SLF asymmetry is directly related to the acuity of AP and musical expertise.

The present data is in accordance with the literature pointing out the special role of the left hemispheric auditory processing by means of structural (Schlaug et al., 1995a; Keenan et al., 2001; Lüders et al., 2004) and functional plasticity (Pantev et al., 1998; Ohnishi et al., 2001; Oechslin et al., 2010) modulated by the level of musical exper-

[1]With one single exception: mean FA-values of C's left hemispheric SLF ROI are significantly correlated with age ($r = 0.573$*, $p = 0.041$).

tise and AP in particular: Generally speaking, the finding concerning the significant interaction *hemisphere* × *expertise* indicates substantial anatomical between-group differences in terms of measuring white matter properties of the SLF core structure irrespective of what we know about FA-values. However, taking into account that in principle relatively high anisotropy is associated with increased diffusivity (Hagmann et al., 2006b) when focusing on neural populations with a high degree of parallel aligned fibres (like in the core of the SLF) we can conclude, that AP musicians obviously show a stronger connectivity of axonal projections within the left SLF than in the right SLF, whereas NM show a vice-versa relationship and RP show no hemispheric difference. With respect to the above mentioned structural and functional hemispheric preponderance of auditory signal processing in musical experts, the present findings seem intriguingly to introduce a developmental specialization of the left SLF architecture by means of an enhanced fibre connectivity and thus information transfer in musicians with AP.

MULTIPLE REGRESSION EFFECTS

Our study sought to investigate AP-specific anisotropic distributions in the SLF structure, the results of the multiple regression revealing an interesting pattern. This comprised three left-lateralized clusters in which FA values correlated positively with the error rates of the AP-musicians such that low FA values correspond with high performances in the AP-test. That these clusters were located at important areas of the SLF architecture and of language processing (Glasser and Rilling, 2008) leads us to assume that this structural asymmetry might have functional implications.

We begin by discussing the two clusters that are part of the arcuate branch of the SLF (**Figures 5B,C**). One of these was located at the superior border of the frontoparietal connection (AF) and is conspicuous by its vicinity to the inferior parietal region, whereas the second was located deep inside the frontal arcuate bundle as it projects into the frontal operculum. Recent observations demonstrate that these latter two cortical grey matter regions are involved in action-related sound recognition (Lahav et al., 2007). In this study, these two regions were activated simultaneously when listening to a newly acquired piece of music, but only in NM. Of course, this function of audio-motor integration is one of the most important aspects of AP, both with respect to acquisition of AP *and* daily practice by AP-musicians. This rare group of musicians most likely associates any heard musical pitch with the corresponding finger position on the instrument. It is thus reasonable to assume that these two clusters are unique to musicians with AP, presumably reflecting AP's exceptional associative linkage between auditory and motor function.

The third SLF cluster was functionally associated with the posterior auditory cortex, and projects to the posterior STG, the superior temporal sulcus (STS), and the MTG (**Figure 5D**). Although evaluation of the exact fibre termination was not possible, the role in speech and auditory processing of the terminal zones of the SLF is undisputed (Buchsbaum et al., 2001; Vigneau et al., 2006). In favour of our interpretation, a recent DTI study identified two distinct SLF pathways in the left hemisphere projecting to language-related cortical areas that both connect the inferior-frontal area with the posterior perisylvian region and the middle-temporal region, (Glasser and Rilling, 2008). In this study, tractography results were compared with peak activation coordinates from prior functional imaging studies. In particular, the authors compared the volumes of the identified pathways between left and right hemisphere. Grey matter STG terminations of the SLF were found to be strongly left lateralized and associated with phonological activations in the left but not in the right hemisphere. Similarly, the MTG terminations were also found to be strongly left lateralized, overlapping in this case with activations associated with lexical semantic activations. Even if these findings are not specifically related to musical expertise, our data are well in line with a previous paper of our group (Oechslin et al., 2010) that reported modulation of activation in brain areas involved in higher language processing by musical expertise and AP. More specifically, musical expertise (AP in contrast to NM) was associated with functional alterations in the posterior parts of the left hemispheric MTG and STS. Given the consistency of this data with that of the current study, we suggest a relationship between local FA values and AP ability that reflects a strong link between musical expertise, AP, and language processing.

NEURAL FORMATION AND AXONAL MYELINATION

In the following, we specify the rationale behind our hypothesis that this lateralization effect is a core feature of AP and based on primal neural formation and myelination of the AF, as part of the SLF, possibly evident long before these individuals become aware of AP.

We now discuss this issue more comprehensively in order to subsequently put forward what we term the *Pioneer Axon Thesis* (**Figure 6** depicts a schematic illustration of different possible organizational principles of the architecture of the arcuate fibre bundle). The principles of axonal guidance have been well investigated (Sperry, 1963; Tessier-Lavigne and Goodman, 1996; Yu and Bargmann, 2001; Guan and Rao, 2003). But the current lack of histological longitudinal studies of white matter development during critical periods of brain development means that, as far as we know, no studies have yet addressed the architectural fibre arrangement of white matter fasciculi in the human brain. But several DTI studies have focused on the development of white matter in different stages of maturation: in premature newborns (Partridge et al., 2004, 2005), during the first 2 years of life (Mukherjee et al.,

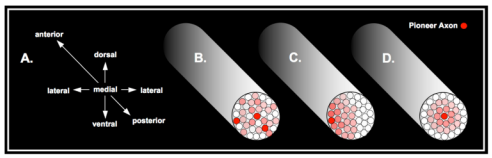

FIGURE 6 | Here a schematic cross-section of the arcuate fasciculus is delineated. On the left **(A)** the orientation of the fasciculus are defined by three axes anterior–posterior, dorsal–ventral and lateral–medial. The second to the left scheme **(B)** represents a chaotic distribution of axonal fibres, with several possible arbitrary positions of the pioneer axon, whereas the increased red colour typifies older axonal pathways. The second to the right scheme **(C)** stands for a possible alternative order driven by a laterally oriented axonal architecture. At the right scheme **(D)**, the proposed architecture due to the maturation of the fasciculus is outlined as suggested by the *Pioneer Axon Thesis* – thus, the pioneer axon is located medially.

2002; Schneider et al., 2004; Gao et al., 2009) and in later life and adolescence (Schmithorst et al., 2002; Snook et al., 2005, 2007). In investigating different DTI parameters like FA, radial and axial diffusivities, these studies provide important data on early maturation and myelination of different white matter structures in the developing brain. The study of cytological and quantitative aspects of callosal axon addition and elimination in rhesus monkey (LaMantia and Rakic, 1990) has shown axon addition occurring exclusively during the period of midgestation through to birth and elimination of about 70% of the callosal axons 4 months after birth. And, in a study that focused on the frontal and the temporal lobe in human brains, a linear degeneration of white matter volume that continued into the fifth decade of life was demonstrated (Bartzokis et al., 2001).

However, it is in postnatal life that reduced tortuosity towards a more straightened, parallel and dense fibre architecture as a function of aging emerges (Takahashi et al., 2000; Paus, 2005; Ashtari et al., 2007). Fibre orientations especially in the SLF have been revealed to be rather random in neonates and to show gradual organization along the anterior–posterior orientation during development (Zhang et al., 2007). Most importantly, of the language-related regions (involved in both perception and production), the AF matures last in terms of myelination (posterior sylvian region, Broca's area, primary motor cortex, primary visual cortex, primary auditory cortex and visual–auditory transition area – gyrus angularis). The pace of myelination of the AF in particular is reported to be similar to these language-related regions, but decelerates after 3 years of age (Su et al., 2008). This characteristic pattern of slow progression of the AF appears to be strongly linked to language acquisition and an age-related increase in vocabulary (Kuhl, 2004; Pujol et al., 2006; Zhang et al., 2007). This is in line with important findings that the associative parietal and temporal fasciculi are the last structures to commence myelination, showing a protracted course into adulthood (Paus et al., 1999; Dubois et al., 2008). In general, myelination processes actually affect diffusion characteristics that are considered to continue over a relatively long period of life: Using *in vivo* morphometry in 111 children (aged 4–17 years), the left AF was found to correlate positively between age and white matter density (Paus et al., 1999). According to these authors, the parameter density reflects increases in axon diameter, myelination or iron concentration, separately or in combination. Cross-section DTI studies of children and adolescents revealed that FA values are significantly positively correlated with age in the language-relevant structures STG, MTG and STS (Barnea-Goraly et al., 2005) and left AF (Schmithorst et al., 2002; Ashtari et al., 2007).

But there is to our knowledge no data on which basis the local fibre arrangement may be interpreted as an expression of cortical maturation within single white matter structures. We therefore propose the *Pioneer Axon Thesis* as a tentative approach for interpreting our DTI data within the context of axonal development and the organizational principles underlying the formation of major white matter pathways like the AF.

We propose a link between axonal arrangements and myelination processes: Since the axonal connections are terminated very early in postnatal life compared with long-lasting myelination processes, we assume that this developmental asynchronicity has a considerable impact on local anisotropic properties of white matter pathways; we assume that early-established, core axonal connections are characterized by diverging diffusion qualities compared with more distal pathway sites, which, according to the cited literature in the preceding, undergo plastic change over a long period of time into adult life.

In general, we suggest there may be a number of different axonal arrangements which may occur in the process of forming a white matter pathway: a random pattern of arrangement may occur in which the pioneer axon could be localized at any possible site within the fasciculus, as illustrated in **Figure 6B**. **Figure 6C** illustrates any possible lateral position of the pioneer axon, all other subsequently developed axons having a clear spatial relation. The manifest architecture is characterized by a consistently laterally oriented pattern of fibre maturation. **Figure 6D** depicts a fibre arrangement, which, from our point of view, is the most likely for a number of reasons outlined in the following. Here, the pioneer axon is located medially, whereas the subsequently formed axons build a concentric architecture as a function of maturation and time.

Given that an initial neural connection between two cortical regions is built up by a pioneer axon, subsequent guided axons will appear according to the relevance and frequency of an innervated connection. Even though future axon generations – ultimately making up a proper fasciculus – arrange themselves in a random pattern, it is reasonable to assume that these axons tend to maintain a certain proximity to the ancestral axons. It is conceivable that this tendency most probably ensures an efficient and preferentially targeted connection between two cortical regions (in case of the AF: the connection between inferior-frontal and temporoparietal/temporal regions). It follows from this that spatial aspects play a major role in the final architecture. Irrespective of axon diameter, an arrangement has to be considered that allows a smooth coexistence of parallel-aligned axons especially in view of the reduction in disposable space over the protracted course of myelination. In summary, compared with earlier generations of axons later generations are forced to choose a trajectory that is radially more distant from the pioneer axon but still as close as possible. Consequently, these processes would yield a concentric architecture reflecting the developmental course of a white matter pathway as illustrated in **Figure 6D**.

In assuming that white matter expansion may occur as a function of learning history, we interpret our DTI data as follows in the context of the proposed mechanism of neural formation and myelination. The implication of this for musical expertise and particularly AP is that there may be a link between expertise and certain anisotropic alterations that may be distinguishable in location and characteristics from earlier (pre-expertise) developed parts of the SLF.

INTEGRATION OF THE PIONEER AXON THESIS

The fact that the ROIs (**Figure 3**) were created by thresholding the probability maps ($p < 0.05$) corroborates the suggestion that the identified ROIs represent ontogenetically earlier sections of the AF, but this does not apply for the localization on the anterior–posterior axis. This is because the six positions of the identified ROIs (3 groups × 2 hemispheres, **Figure 3**) depend on the two intersectional ROIs that were used to track the SLF of single

subjects (**Figure 1**), which in turn form the basis for creating probability maps. In this context, the essential role of DTI probability maps might be clearer by referring to their main attribute; because high probability for local (voxelwise) fibre occurrence is a consequence of low inter-individual variability of fibre presence. Since in the AF high inter-individual morphological variations are assumed to develop at later stages of cortical maturation, we suggest that structures with very low inter-individual variability and high morphological consistency tend to develop in very early maturational stages. This argumentation is supported by a longitudinal study of grey matter maturation that demonstrated a heterochronous pattern of cortical development (Gogtay et al., 2004): In general, the data lead the authors to suggest that phylogenetical older cortical areas mature earlier compared with more recent evolved cortical regions.

As the identified ROIs of SLF (**Figure 3**) represent the regions of lowest inter-individual variability, a plausible explanation is that ontogenetically early fibre tracts characterize the core section of a gross pathway like the AF. This conclusion is consistent with our *Pioneer Axon Thesis*, which presumes that the underlying architecture of a white matter pathway is determined by a concentric axonal arrangement that reflects the process of cortical maturation and the following spatio-temporal pattern of myelination.

In view of the local arrangement of both the identified ROI of APs left hemispheric SLF and the identified cluster (the latter representing voxels with a significant negative correlation between FA-values and AP-test error-rate), it is clear that the ROI (red coloured) is located at the core of the SLF, whereas the identified cluster (golden coloured, also in **Figure 5B**) is located at the boarder of the SLF (**Figure 6**).

We assume therefore that the group-specific lateralization effect (**Figure 7**, red coloured, core arcuate region) putatively reflects an earlier developmental stage before and during deliberate musical practice (pre-expertise-state). In addition, we identified by multiple regression a distinctive peripheral cluster (**Figure 7**, golden coloured, superior border arcuate region) which might be associated with plastic changes following later acquired musical expertise and AP. This would be consistent with a DTI study (McGraw et al., 2002) that compared compact white matter (corpus callosum, interne capsule, cerebral peduncle) with non-compact white matter (corona radiata and peripheral white matter). These authors suggested that myelination is initially greater in compact white matter, whereas the change in myelination may be greater in non-compact white matter during early childhood. Moreover, our data lead us to suggest that a specific local anisotropic lateralization, characterizing the early matured compact core of the SLF, underpins the development of AP under favourable environmental conditions, such as an early start to musical training and deliberate practice (Baharloo et al., 1998; Vitouch, 2003).

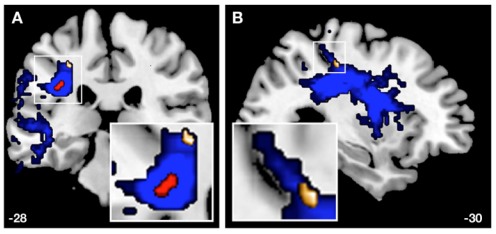

FIGURE 7 | A coronal (A) and a sagittal (B) view of the probability map of the APs' left SLF are illustrated (blue). The red cluster represents the overlaid ROI (**Figure 3**) due to the thresholded probability map ($p < 0.05$), whereas the golden cluster (see also **Figure 5B**) represents voxels of FA values (–28, –28, 44) that are significantly correlated ($r = 0.758^{**}$) with the error rates of APs with respect to the AP-test.

Alternatively, we cannot rule out the possibility that the demonstrated anisotropic lateralization effects even in the core arcuate structure are due to plastic changes as a function of deliberate practice and musical expertise. But it is plausible to assume on the basis of our considerations and argumentation that effects of core white matter anisotropic characteristics more likely reflect the impact of earlier ontogenetic stages of development than do peripheral group-specific alterations.

On might be concerned about the strength of the statistical effects. Certainly it would have been desirable to investigate larger sample of musicians and NM, to end up with more robust statistical effects. However, given the rare incidence of AP musicians in the population the present sample size ($n = 13$ per group) should by all means considered a reasonable and representative number.

Second, since our study emphasizes a relationship between differences in structural architecture as a function of musical expertise and its implications for auditory and speech functions it would have been wishful to compare brain imaging data with behavioural data obtained from measurements of language proficiency. However to the best of our knowledge a suitable behavioural screening that covers a broad range of speech and language functions does not exist.

CONCLUSIONS

In summarizing our results, we conclude first that musical expertise combined with AP leads to a left-sided lateralization of mean FA-values among the core structures of the AF, as identified on the basis of high inter-individual morphological congruency. This effect is modulated considerably by the level of musical expertise (significant interaction *musical expertise* × *hemisphere*), since RP musicians revealed no inter-hemispheric differences. Obviously, the anisotropic properties of the selected SLF section represent a marked discriminatory feature of musical expertise and AP respectively.

Secondly, we identified three distinctive clusters exclusively in the left SLF in AP musicians, whose FA-values correlated positively with the error rate evaluated by the AP-test. This proficiency effect was not present in RP musicians. In other words, the higher the AP acuity in AP musicians the lower are the FA values within the identified three regions, two of which (**Figures 5C,D**) play an prominent role in language processing (Glasser and Rilling, 2008).

Thirdly, the *Pioneer Axon Thesis* proposes that peripheral white matter development (contrary to compact white matter core regions) is influenced considerably by environmental factors, in this case musical training, over a long period in postnatal life. Thus, deliberate music practice, which is the *sine qua non* of the acuity of AP, might be quantifiable in the form of particular alterations in white matter plasticity of auditory-related fasciculi like the SLF.

With respect to the long-lasting debate as to whether AP is acquired or genetically disposed, further DTI studies would facilitate the investigation of familial aggregation of anisotropic characteristics within the early developing region of the arcuate core. If our suggestion holds true, a musician's family with many AP members should be separable from a musician's family without AP members. In fact, such an approach might provide a better understanding of the interaction of genetics and environmental factors that contribute to the manifestation of AP.

ACKNOWLEDGMENTS

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4. Discussion

4.1. Study 1

Based on recent studies (Magne et al., 2006; Schön et al., 2004; Patrick C M Wong, Skoe, Russo, Dees, & Kraus, 2007) one might expect an enhanced sensitivity for pitch contours in musicians during prosodic speech processing. However, the present study did not reveal a significant main effect when prosody is manipulated (Table 1[1]: main effect [ME] segmental). Notably, as the methodological approaches (event related potentials, brainstem-potentials) and tasks in aforementioned studies clearly differ from the introduced design it is difficult to compare the results, last but not least due to temporal constraints associated with fMRI and the BOLD signal. Unlike the previously mentioned electroencephalography (EEG) studies, the fMRI technique focuses on quite different time frames due to coarser resolution during cortical speech processing. Given the results of these studies, the question may be raised whether AP musicians show an exceptional sensitivity for prosodic processing - however, AP should be considered a phenomenon that differs from standard musical proficiency (which is the subject of investigation in the above cited studies) and may not imply an enhanced sensitivity to prosodic information.

4.1.1. The main effect of *expertise*

In the statistical analysis the main effect of *expertise* is characterized by bilateral activation on the superior temporal plane with a slight right-hemispheric preponderance (MS: Fig. 2A). Musical expertise, irrespective of whether the presented stimuli contained prosodic/lexical information does not account for this finding. The activation pattern is characterized as follows: the higher the musical training - in particular with respect to AP - the lower the activation in the specific region of primary auditory information processing. Accordingly, musical expertise is the main driving factor explaining different activations in the core auditory regions, thus extending recent findings of other research groups (P. Schneider et al., 2002; P. C. M. Wong et al., 2008).

[1] All indexes of figures and tables in the discussion section are referring to the published papers.

4.1.2. Discussion of the results in the context of the neural efficiency hypothesis

The main effect of *expertise* possibly indicates more efficient processing by the auditory cortex as a function of musical proficiency. Using EEG, positron emission tomography, and fMRI, the principles of neural efficiency have been discussed within several different contexts such as spatial perception (O Vitouch, Bauer, Gittler, Leodolter, & Leodolter, 1997), superior cognitive performance by figural intelligence in chess players (Grabner, Neubauer, & Stern, 2006) and working memory (Grabner, Stern, & Neubauer, 2003). The data provided by these studies imply that higher performance levels are associated with lower cortical activations. Additionally, this relationship has been found (Haier, Siegel, Tang, Lennart, & Buchsbaum, 1992) even as a consequence of ‘‘Tetris’’ learning effects, which were associated with a decrease of local glucose metabolic rates. In general, these authors propose that ‘‘brighter’’ (or more proficient) subjects have to invest less cortical resources to achieve accurate performances. Conversely, cognitively less proficient subjects had to invest more cortical resources to solve the same tasks. From an anatomical point of view, it has been demonstrated, that more gray matter in distinct cortical regions (primary auditory cortex and PT amongst others) is associated with higher IQs; more gray matter also results in less use of energy, when the area is engaged (efficiently) in specific cognitive tasks (Haier, Jung, Yeo, Head, & Alkire, 2004).

This argumentation is in line with studies focusing on sensory information processing in the visual cortex (Marcar, Straessle, Girard, Loenneker, & Martin, 2004). The standard model put forward by these authors holds that an increase in the electrical activity and an increase in size of the activated neural population have an opposing influence on the BOLD signal amplitude (Marcar & Loenneker, 2004). In a nutshell, this model states that the vascular response is controlled by electrical discharge activity, whereas the oxygen consumption is dependent on the size of the activated neuronal population. Based on an experimental MR setting different checkerboard patterns were presented (flashed vs. reversing), whereas the size of activated neural populations has been manipulated (Marcar, Strassle, Loenneker, Schwarz, & Martin, 2004). The results demonstrated that the checkerboard that is associated with a lower neural activity yielded a larger number of activated voxels and a stronger BOLD response.

These results are contradictory to the Linear Transfer Model, which states that the BOLD contrast signal is directly proportional to the neuronal activity.

In the context of language comprehension, it has been demonstrated that the neural correlates of semantic priming support the neural efficiency hypothesis (Rissman, Eliassen, & Blumstein, 2003): Semantically related word pairs showed consistently less activation than unrelated pairs—interestingly, with respect to the temporal lobe this activation pattern is restricted to the left STG, and does not affect the MTG. As the authors argue, the perception of a prime word activates a lexical--semantic network that shares common elements with the target word, and, thus, the target can be recognized with enhanced neural efficiency. The proposed relationship between STG and MTG is striking, because the MTG - which doubtlessly is crucial for lexical-semantic processes - does not contribute to the pattern of neural efficiency, drawn by the recruitment of the neural population, which is responsible for primary auditory signal decoding.

Furthermore, in interpreting the main effect of *expertise*, which is characterized by lowest activation of the STG bilaterally in AP and highest activations in NM, it might be useful to recall the characteristic morphological lateralization of Heschl's Gyrus (P. Schneider et al., 2005) in professional musicians and the PT in professional musicians with AP (Keenan et al., 2001; Schlaug, Jäncke et al., 1995). Due to an increased size of these structures in the left hemisphere, it seems reasonable to assume that they subserve auditory processing by means of an optimal contribution, characterized by the above- discussed neural efficiency hypothesis. Thus, the revealed main effect of *expertise* can be taken to be the first evidence for neural efficiency in basal auditory processing of language as a function of musical expertise.

4.1.3. The main effect *suprasegmental*

When considering the main effect *suprasegmental*, left temporal brain areas comprising posterior parts of the STG, STS, MTG, and ITG are more strongly activated during processing of lexical and propositional information (MS: Fig. 3B). Consistent with this is the finding that the posterior MTG and the lower bank of the posterior STS are involved in lexical and phonetic analyses (Binder et al., 2000; Dick et al., 2007). Essentially, many authors of clinical and nonclinical studies have maintained that the left MTG plays a specific role in lexical and semantic processing (Binder et al., 2000; Dick et al., 2007). By applying voxel-based lesion-symptom

mapping it has been shown that the posterior MTG is one of the main areas involved in higher-order language processing (Bates et al., 2003; Dronkers, Wilkins, Valin, Redfern, & Jaeger, 2004). In addition, functional neuroimaging studies support the special role of the posterior MTG in language processing. At least one study that investigated word ambiguity (Rodd, Davis, & Johnsrude, 2005) showed elegantly the involvement of the posterior MTG in semantic analyses. Accordingly, there should be a strong link between the auditory cortex and the posterior MTG during lexical information processing. Therefore, both the auditory cortex and the MTG are essential for a proper distinguishing between the words *beer* and *peer*.

4.1.4. The interaction *suprasegmental* x *expertise*

With respect to the above-mentioned context I found a strong interaction between the factors *suprasegmental* and *expertise* located in the left MTG, which is characterized by stronger responses to lexical compared with delexicalized information, with musicians showing the strongest difference. With respect to the main effect expertise this activation pattern does not conflict with the above-discussed efficiency hypothesis. As already mentioned, due to the cortical recruitment of lexical-semantic networks it has been demonstrated that primary auditory processing is driven by the principles of neural efficiency, whereas the activity of the MTG shows a different activation pattern which cannot be explained using this line of argumentation. Nevertheless, the MTG provides core evidence for lexical-semantic processing (Rissman et al., 2003).

In general, these results are also in line with the dual stream model (Hickok & Poeppel, 2007) that postulates a lexical interface located in the posterior part of the left MTG.

Contrary to strong left-sided activations of the posterior STS due to segmental speech processing (Friederici & Alter, 2004), activations of the posterior MTG are specific to musicianship, with musicians (with AP or RP) demonstrating stronger bilateral hemodynamic responses compared with nonmusicians. According to the 2-way ANOVAs (motivated by the findings due to the expertise 3 suprasegmental interaction, Fig. 1), the main effect expertise in both delexicalized and non-delexicalized conditions lets us suggest that the MTG might be crucial for higher-level language processing. The post hoc tests show a significant enhancement of effect sizes in this area in musicians compared with nonmusicians (MS: Fig. 4C). In

addition, the analysis of posterior STS (MS: Fig. 4C) revealed that AP musicians show stronger left lateralized activations during processing of segmental information compared with the other 2 groups. This finding is in line with several reports of left-sided enhanced levels of activation in AP musicians during complex auditory tasks (Itoh et al., 2005; Ohnishi et al., 2001; Pantev et al., 1998). Based on these findings, it is proposed that the auditory acuity of AP is not limited to basal auditory processing (usually conceived in terms of music processing), but extends to a more general notion of acoustic segmentation by fully integrating left-hemispheric speech-relevant networks.

4.1.5. Conclusion of Study 1

Taken together, the introduced fMRI study presents 2 novel findings: First, there is an AP-specific enhancement of the left lateralized activation in the lower bank of the posterior STS for segmental speech processing; second, musicians generally demonstrate stronger bilateral BOLD effects in the posterior MTG in all conditions. In addition, this effect of segmental processing is substantially enhanced in AP musicians compared with the other 2 experimental groups. This novel insights let conclude that neurofunctional alterations due to musicianship are not only manifested in exceptional acuity of music processing, but also affect speech processing in the sense that AP represents a comprehensive analytical proficiency for acoustic signal decoding.

4.2. Study 2

This study focused on alterations in white matter as a function of musical training and exceptional hearing abilities. The specific interest, as outlined in the introduction and reflected in the introduced analysis, concerned whether and to what extent there are differences in FA-values within the SLF structure between (i) musicians and non-musicians, and (ii) between musicians with and without AP. Firstly, we discuss ROI-based effects of hemispheric lateralisations that reflect between-group differences. Secondly, our discussion emphasizes AP-specific FA characteristics for the SLF as a whole. Finally, we discuss our results in the context of myelination principles and axonal formation and we introduce the *Pioneer Axon Thesis*.

4.2.1. ROI analysis due to probability maps

The utilization of group-specific probability maps for ROI generation revealed a lateralization effect as a function of musical expertise (as revealed by the ANOVA). We found greater left than right lateralization of mean FA values in AP and greater right than left lateralization in NM, while there was no significant lateralization effect in RP. In contrast, the analysis of the complete structure of SLF, by averaging FA values of all corresponding voxels (Fig. 4), revealed no significant lateralization effect as a function of musical expertise.

The group-specific lateralization of mean FA values (Figure 3) cannot be explained by differences in the biographic variables age, onset of musical training, or total amount of practice years (Table 1). The inclusion of these biographical parameters - both partial (corrected for age) and bivariate - in our correlational approach allows us to rule out any significant relationship between these demographic parameters[2] and mean FA values within the ROIs of the left/right hemisphere in all three groups. A meaningful influence of these factors on the demonstrated group-specific lateralization effects appears unlikely. The significant interaction *expertise* x *hemisphere* and the results of post-hoc *t*-tests suggest that the SLF asymmetry is directly related to the acuity of AP and musical expertise.

The present data is in accordance with the literature pointing out the special role of the left hemispheric auditory processing by means of structural (Schlaug, et al., 1995; Keenan, et al., 2001; Lüders et al. 2004) and functional plasticity (Pantev et al., 1998; Ohnishi et al., 2001; Oechslin et al., 2009) modulated by the level of musical expertise and AP in particular: Generally speaking, the finding concerning the significant interaction *Hemisphere* x *Expertise* indicates substantial anatomical between-group differences in terms of measuring white matter properties of the SLF core structure irrespective of what we know about FA-values. However, taking into account that in principle relatively high anisotropy is associated with increased diffusivity (Hagmann et al. 2006b) when focusing on neural populations with a high degree of parallel aligned fibers (like in the core of the SLF) we can conclude, that AP musicians obviously show a stronger connectivity of axonal projections within the

[2] With one single exception: mean FA-values of C's left hemispheric SLF ROI are significantly correlated with age (r = 0.573*, p = 0.041).

left SLF than in the right SLF, whereas non-musicians show a vice-versa relationship and RP show no hemispheric difference. With respect to the above mentioned structural and functional hemispheric preponderance of auditory signal processing in musical experts, the present findings seem intriguingly to introduce a developmental specialization of the left SLF architecture by means of an enhanced fiber connectivity and thus information transfer in musicians with AP.

4.2.2. Multiple regression effects

This study sought to investigate AP-specific anisotropic distributions in the SLF structure, the results of the multiple regression reveal an interesting pattern. This comprised three left-lateralized clusters in which FA values correlated positively with the error rates of the AP-musicians such that low FA values correspond with high performances in the AP-test. That these clusters were located at important areas of the SLF architecture and of language processing (Glasser & Rilling, 2008) leads us to assume that this structural asymmetry might have functional implications.

We begin by discussing the two clusters that are part of the arcuate branch of the SLF (Figure 5.B, 5.C). One of these was located at the superior border of the frontoparietal connection (arcuate fasciculus) and is conspicuous by its vicinity to the inferior parietal region, whereas the second was located deep inside the frontal arcuate bundle as it projects into the frontal operculum. Recent observations demonstrate that these latter two cortical grey matter regions are involved in action-related sound recognition (Lahav, Saltzman, & Schlaug, 2007). In this study, these two regions were activated simultaneously when listening to a newly acquired piece of music, but only in non-musicians. Of course, this function of audio-motor integration is one of the most important aspects of AP, both with respect to acquisition of AP *and* daily practice by AP-musicians. This rare group of musicians most likely associates any heard musical pitch with the corresponding finger position on the instrument. It is thus reasonable to assume that these two clusters are unique to musicians with AP, presumably reflecting AP's exceptional associative linkage between auditory and motor function.

The third SLF cluster was functionally associated with the posterior auditory cortex, and projects to the posterior superior temporal gyrus (STG), the superior temporal sulcus (STS), and the middle temporal gyrus (MTG) (Figure 5.D). Although

evaluation of the exact fiber termination was not possible, the role in speech and auditory processing of the terminal zones of the SLF is undisputed (Buchsbaum, Hickok, & Humphries, 2001). In favor of our interpretation, a recent DTI study identified two distinct SLF pathways in the left hemisphere projecting to language-related cortical areas that both connect the inferior-frontal area with the posterior perisylvian region and the middle-temporal region, (Glasser & Rilling, 2008). In this study, tractography results were compared with peak activation coordinates from prior functional imaging studies. In particular, the authors compared the volumes of the identified pathways between left and right hemisphere. Grey matter STG terminations of the SLF were found to be strongly left lateralized and associated with phonological activations in the left but not in the right hemisphere. Similarly, the MTG terminations were also found to be strongly left lateralized, overlapping in this case with activations associated with lexical semantic activations. Even if these findings are not specifically related to musical expertise, our data are well in line with a previous paper of our group (Oechslin et al., 2009) that reported modulation of activation in brain areas involved in higher language processing by musical expertise and AP. More specifically, musical expertise (AP in contrast to NM) was associated with functional alterations in the posterior parts of the left hemispheric MTG and STS. Given the consistency of this data with that of the current study, we suggest a relationship between local FA values and AP ability that reflects a strong link between musical expertise, AP, and language processing.

4.2.3. Neural formation and axonal myelination

In the following, we specify the rationale behind our hypothesis that this lateralization effect is a core feature of AP and based on primal neural formation and myelination of the arcuate fasciculus, as part of the SLF, possibly evident long before these individuals become aware of AP.

We now discuss this issue more comprehensively in order to subsequently put forward what we term the *Pioneer Axon Thesis* (Figure 6 depicts a schematic illustration of different possible organizational principles of the architecture of the arcuate fiber bundle). The principles of axonal guidance have been well investigated (Guan & Rao, 2003; Sperry, 1963; Tessier-Lavigne & Goodman, 1996; Yu & Bargmann, 2001). But the current lack of histological longitudinal studies of white

matter development during critical periods of brain development means that, as far as we know, no studies have as yet, addressed the architectural fiber arrangement of white matter fasciculi in the human brain. But several DTI studies have focused on the development of white matter in different stages of maturation: in premature newborns (Partridge et al., 2005; Partridge et al., 2004), during the first 2 years of life (Gao et al., 2009; Mukherjee et al., 2002; J. F. Schneider, Il'yasov, Hennig, & Martin, 2004) and in later life and adolescence (Schmithorst, Wilke, Dardzinski, & Holland, 2002; Snook, Paulson, Roy, Phillips, & Beaulieu, 2005; Snook, Plewes, & Beaulieu, 2007). In investigating different DTI parameters like FA, radial and axial diffusivities, these studies provide important data on early maturation and myelination of different white matter structures in the developing brain. The study of cytological and quantitative aspects of callosal axon addition and elimination in rhesus monkey (LaMantia & Rakic, 1990) has shown axon addition occurring exclusively during the period of midgestation through to birth and elimination of about 70% of the callosal axons 4 months after birth. And, in a study that focused on the frontal and the temporal lobe in human brains, a linear degeneration of white matter volume that continued into the 5th decade of life was demonstrated (Bartzokis et al., 2001).

However, it is in postnatal life that reduced tortuosity toward a more straightened, parallel and dense fiber architecture as a function of aging emerges (Ashtari et al., 2007; Paus, 2005; Takahashi, Ono, Harada, Maeda, & Hackney, 2000). Fiber orientations especially in the SLF have been revealed to be rather random in neonates and to show gradual organization along the anterior-posterior orientation during development (Zhang et al., 2007). Most importantly, of the language-related regions (involved in both perception and production), the arcuate fasciculus matures last in terms of myelination (posterior sylvian region, Broca's area, primary motor cortex, primary visual cortex, primary auditory cortex and visual-auditory transition area - gyrus angularis). The pace of myelination of the arcuate fasciculus in particular is reported to be similar to these language-related regions, but decelerates after 3 years of age (Su, Kuan, Kaga, Sano, & Mima, 2008). This characteristic pattern of slow progression of the arcuate fasciculus appears to be strongly linked to language acquisition and an age-related increase in vocabulary (Kuhl, 2004; Pujol et al., 2006; Zhang et al., 2007). This is in line with important findings that the associative parietal and temporal fasciculi are the last structures to commence myelination, showing a

protracted course into adulthood (Dubois et al., 2008; Paus et al., 1999). In general, myelination processes actually affect diffusion characteristics that are considered to continue over a relatively long period of life: Using in vivo morphometry in 111 children (aged 4 to 17 years), the left arcuate fasciculus was found to correlate positively between age and white matter density (Paus et al., 1999). According to these authors, the parameter density reflects increases in axon diameter, myelination or iron concentration, separately or in combination. Cross-section DTI studies of children and adolescents revealed that FA values are significantly positively correlated with age in the language-relevant structures STG, MTG and STS (Barnea-Goraly et al., 2005) and left arcuate fasciculus (Ashtari et al., 2007; Schmithorst et al., 2002).

But there is to our knowledge no data on which basis the local fiber arrangement may be interpreted as an expression of cortical maturation within single white matter structures. We therefore propose the *Pioneer Axon Thesis* as a tentative approach to interpreting our DTI data within the context of axonal development and the organizational principles underlying the formation of major white matter pathways like the arcuate fasciculus.

We propose a link between axonal arrangements and myelination processes: Since the axonal connections are terminated very early in postnatal life compared with long-lasting myelination processes, we assume that this developmental asynchronicity has a considerable impact on local anisotropic properties of white matter pathways; we assume that early-established, core axonal connections are characterized by diverging diffusion qualities compared with more distal pathway sites, which, according to the cited literature in the preceding, undergo plastic change over a long period of time into adult life.

In general, we suggest there may be a number of different axonal arrangements which may occur in the process of forming a white matter pathway: a random pattern of arrangement may occur in which the pioneer axon could be localized at any possible site within the fasciculus, as illustrated in Fig. 6.B.. Fig 6.C. illustrates any possible lateral position of the pioneer axon, all other subsequently developed axons having a clear spatial relation. The manifest architecture is characterized by a consistently laterally-oriented pattern of fiber maturation. Fig 6.D depicts a fiber

arrangement, which, from our point of view, is the most likely for a number of reasons outlined in the following. Here, the pioneer axon is located medially, whereas the subsequently formed axons build a concentric architecture as a function of maturation and time.

Given that an initial neural connection between two cortical regions is built up by a pioneer axon, subsequent guided axons will appear according to the relevance and frequency of an innervated connection. Even though future axon generations – ultimately making up a proper fasciculus – arrange themselves in a random pattern, it is reasonable to assume that these axons tend to maintain a certain proximity to the ancestral axons. It is conceivable that this tendency most probably ensures an efficient and preferentially targeted connection between two cortical regions (in case of the arcuate fasciculus: the connection between inferior-frontal and temporo-parietal/temporal regions). It follows from this that spatial aspects play a major role in the final architecture. Irrespective of axon diameter, an arrangement has to be considered that allows a smooth coexistence of parallel-aligned axons especially in view of the reduction in disposable space over the protracted course of myelination. In summary, compared with earlier generations of axons later generations are forced to choose a trajectory that is radially more distant from the pioneer axon but still as close as possible. Consequently, these processes would yield a concentric architecture reflecting the developmental course of a white matter pathway as illustrated in Fig. 6D.

In assuming that white matter expansion may occur as a function of learning history, we interpret our DTI data as follows in the context of the proposed mechanism of neural formation and myelination. The implication of this for musical expertise and particularly AP is that there may be a link between expertise and certain anisotropic alterations that may be distinguishable in location and characteristics from earlier (pre-expertise) developed parts of the SLF.

4.2.4. Integration of the Pioneer Axon Thesis

The fact that the ROIs (Fig. 3) were created by thresholding the probability maps ($p < 0.05$) corroborates the suggestion that the identified ROIs represent ontogenetically earlier sections of the arcuate fasciculus, but this does not apply for the localization on the anterior-posterior axis. This is because the six positions of the identified ROIs

(3 groups x 2 hemispheres, Fig. 3) depend on the two intersectional ROIs that were used to track the SLF of single subjects (Fig. 1), which in turn form the basis for creating probability maps. In this context, the essential role of DTI probability maps might be clearer by referring to their main attribute; because high probability for local (voxel-wise) fiber occurrence is a consequence of low inter-individual variability of fiber presence. Since in the AF high inter-individual morphological variations are assumed to develop at later stages of cortical maturation, we suggest that structures with very low inter-individual variability and high morphological consistency tend to develop in very early maturational stages. This argumentation is supported by a longitudinal study of grey matter maturation that demonstrated a heterochronous pattern of cortical development (Gogtay et al., 2004): In general, the data lead the authors to suggest that phylogenetical older cortical areas mature earlier compared with more recent evolved cortical regions.

As the identified ROIs of SLF (Fig. 3) represent the regions of lowest inter-individual variability, a plausible explanation is that ontogenetically early fiber tracts characterize the core section of a gross pathway like the arcuate fasciculus. This conclusion is consistent with our *Pioneer Axon Thesis*, which presumes that the underlying architecture of a white matter pathway is determined by a concentric axonal arrangement that reflects the process of cortical maturation and the following spatio-temporal pattern of myelination.

In view of the local arrangement of both the identified ROI of APs left hemispheric SLF and the identified cluster (the latter representing voxels with a significant negative correlation between FA-values and AP-Test error-rate), it is clear that the ROI (red coloured) is located at the core of the SLF, whereas the identified cluster (golden coloured, also in Figure 5.B.) is located at the boarder of the SLF (Figure 6).

We assume therefore that the group-specific lateralization effect (Figure 7, red coloured, core arcuate region) putatively reflects an earlier developmental stage before and during deliberate musical practice (pre-expertise-state). In addition, we identified by multiple regression a distinctive peripheral cluster (Figure 7, golden coloured, superior border arcuate region), which might be associated with plastic changes following later acquired musical expertise and AP. This would be consistent with a DTI study (McGraw, Liang, & Provenzale, 2002) that compared compact white

matter (corpus callosum, interne capsule, cerebral peduncle) with non-compact white matter (corona radiata and peripheral white matter). These authors suggested that myelination is initially greater in compact white matter, whereas the change in myelination may be greater in non-compact white matter during early childhood. Moreover, our data lead us to suggest that a specific local anisotropic lateralization, characterizing the early matured compact core of the SLF, underpins the development of AP under favorable environmental conditions, such as an early start to musical training and deliberate practice (Baharloo et al., 1998; Oliver Vitouch, 2003).

Alternatively, we cannot rule out the possibility that the demonstrated anisotropic lateralization effects even in the core arcuate structure are due to plastic changes as a function of deliberate practice and musical expertise. But it is plausible to assume on the basis of our considerations and argumentation that effects of core white matter anisotropic characteristics more likely reflect the impact of earlier ontogenetic stages of development than do peripheral group-specific alterations.

On might be concerned about the strength of the statistical effects. Certainly it would have been desirable to investigate larger sample of musicians and non-musicians, to end up with more robust statistical effects. However, given the rare incidence of AP musicians in the population the present sample size (n=13 per group) should by all means considered a reasonable and representative number.

Second, since our study emphasizes a relationship between differences in structural architecture as a function of musical expertise and its implications for auditory and speech functions it would have been wishful to compare brain imaging data with behavioral data obtained from measurements of language proficiency. However to the best of our knowledge a suitable behavioral screening that covers a broad range of speech and language functions does not exist.

4.2.5. Conclusions of Study 2

In summarizing our results, we conclude first that musical expertise combined with AP leads to a left-sided lateralization of mean FA-values among the core structures of the arcuate fasciculus, as identified on the basis of high inter-individual morphological congruency. This effect is considerably modulated by the level of

musical expertise (significant interaction musical *expertise* x *hemisphere*), since RP musicians revealed no inter-hemispheric differences. Obviously, the anisotropic properties of the selected SLF section represent a marked discriminatory feature of musical expertise and AP respectively.

Secondly, we identified 3 distinctive clusters exclusively in the left SLF in AP musicians, whose FA-values correlated positively with the error rate evaluated by the AP-Test. This proficiency effect was not present in RP musicians. In other words, the higher the AP acuity in AP musicians the lower are the FA values within the identified 3 regions, two of which (Fig. 5; C, D) play an prominent role in language processing (Glasser & Rilling, 2008).

Thirdly, the *Pioneer Axon Thesis* proposes that peripheral white matter development (contrary to compact white matter core regions) is influenced considerably by environmental factors, in this case musical training, over a long period in postnatal life. Thus, deliberate music practice, which is the *sine qua non* of the acuity of AP, might be quantifiable in the form of particular alterations in white matter plasticity of auditory-related fasciculi like the SLF.

With respect to the long-lasting debate as to whether AP is acquired or genetically disposed, further DTI studies would facilitate the investigation of familial aggregation of anisotropic characteristics within the early developing region of the arcuate core. If our suggestion holds true, a musician's family with many AP members should be separable from a musician's family without AP members. In fact, such an approach might provide a better understanding of the interaction of genetics and environmental factors that contribute to the manifestation of AP.

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6. Abbreviations

AP: Absolute Pitch

BOLD: Blood Oxygenated Level Dependent

DTI: Diffusion Tensor Imaging

EEG: Electroencephalography

FA: Fractional Anisotropy

fMRI: Functional Magnetic Resonance Imaging

ITG: Inferior Temporal Gyrus

ME: Main Effect

MS: Manuscript

MTG: Middle Temporal Gyrus

NM: Non-musicians

PT: Planum Temporale

RP: Relative Pitch

SD: Standard Deviation

STG: Superior Temporal Gyrus

SLF: Superior Longitudinal Fasciculus

STS: Superior Temporal Sulcus

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- Meyer, M., Elmer S., Ringli, M, **Oechslin**, M.S., Baumann, S., Jäncke L. (in press), *Long-term exposure to music enhances sensitivity of the auditory system in children*, European Journal of Neuroscience.

- **Oechslin**, M.S., Imfeld, A., Loenneker, T., Meyer, M., Jäncke (2010), *The plasticity of the superior longitudinal fasciculus as a function of musical expertise: a diffusion tensor imaging study*, Frontiers in Human Neuroscience, Feb 8; 3:76.

- **Oechslin**, M.S., Meyer, M., Jäncke, (2010), *Absolute pitch - functional evidence for speech-relevant auditory acuity*, Cerebral Cortex, 20(2): 447-55.

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- Hänggi, J., Beeli, G**.,** **Oechslin**, M.S., Jäncke, L., (2008). *The multiple synaesthete E.S. - Neuroantomical basis of interval-taste and tone-color synaesthesia*, NeuroImage, 43(2): 192-203.

- **Oechslin**, M.S., Neukom, M., Bennet, J., (2008), *The Doppler effect - an evolutionary critical cue for the perception of the direction of moving sound sources*, IEEE Association, Proceedings of the International Conference on Audio, Language and Image Processing, Shanghai.

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Other Publications:

- **Oechslin**, M.S. *Neurowissenschaftliche Aspekte einer Akustik des Virtuellen*, in Maeder, M. (Ed.): *Milieux Sonores/Klangliche Millieus*, *Zum Verhältnis von Klang und Raum*, Publisher: *transcript*, June 2010 (English translation appears prospectively in fall 2010).

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Unpublished Master Thesis:

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Poster und Congress abstracts:

- James, C., **Oechslin**, M.S., Van De Ville, D., Lazeyras F., Hauert C.-A., *Musical syntax processing as a function of musical expertise: Part 1: Spatio-temporal ERP analysis*, The Neurosciences and Music IV, Edinburgh (UK), June 9^{th}-12^{th}, 2011.

- **Oechslin,** M.S., Van De Ville, D., Lazeyras F., Hauert C.-A., James C.E., *Musical syntax processing as a function of musical expertise: Part 2: Functional magnetic resonance imaging data*, The Neurosciences and Music IV, Edinburgh (UK), June 9^{th}-12^{th}, 2011.

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- **Oechslin**, M.S., Meyer, M., Jäncke L., *Neural underpinnings of segmental speech processing in musicians with and without absolute pitch*, The Neurosciences and Music III, Disorders and Plasticity, McGill University, Montreal, June 25^{th} - 28^{th}, 2008.

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- Imfeld, A., **Oechslin**, M.S., Loenneker, T., Meyer, M., Jäncke, L., *Neuroantomical images of white matter fiber structures using DTI*, ZNZ Symposium, Sept. 14th, 2007.

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- **Oechslin**, M.S., Baumann S., Oppenheim, I., Meyer, M. & Jäncke, L., *EEG-Evidence for different auditory processing in absolute pitch possessors*. INS Meeting Zurich, July 26th – 30th, 2006.

Symposia:

- **Oechslin,** M.S. (Chair): *Impacts of musical expertise on cerebral language processing*, Symposium 2, The Neuroscience and Music conference IV, Edinburgh (UK), June 10th, 2011.

Invited Talks:

- **Oechslin**, M.S., *Thinking and innovation – when innovation becomes sound*, Swissnex China, Minsheng Art Museum, Shanghai, August 26th , 2010.

- **Oechslin,** M.S., *Die zerebrale Organisation des absoluten Gehörs im Schnittpunkt zwischen Musik und Sprache*, Department of Psychology, Cognitive Psychology Unit, University of Klagenfurt, November 11th, 2009.

- **Oechslin**, M.S., *Cerebral organization of absolute pitch within the framework of speech and music*, Colloque de recherche en orientations cognitive et développementale, Faculté de Psychologie et des Sciences de l'Education, University of Geneva, October 27th, 2009.

- **Oechslin,** M.S., *Functional underpinnings of language processing in musicians with absolute pitch,* ESCOM 09, Iyväskylä, August 12th – 16th, 2009.

- **Oechslin**, M.S., Jäncke, J., *Absolute pitch*, Symposium 3: Musical training and induced cortical plasticity, The Neurosciences and Music III, Disorders and Plasticity, McGill University, Montreal, June 25th - 28th, 2008.

- **Oechslin**, M.S., Neukom, M., Bennett, J., *The Doppler effect - an evolutionary critical cue for the perception of the direction of moving sound sources*, IEEE Conference *ICALIP 2008*, Shanghai, July, 7th - 9th, 2008.

- **Oechslin**, M.S., *Zur neuronalen Verarbeitung von Sprache bei Absoluthörern*, Gastvortrag im Doktoranden - und Lizentiandenkolloquium des Instituts für Allgemeine Psychologie der Universität Zürich, September 26th, 2007.

- **Oechslin**, M.S., Vitouch, O., Damian, *Von Quintenzirkel und Kleinterzproblem – die kognitive Repräsentation von Dur-Dreiklängen bei Musikern*, L., Klagenfurt, *7. Wissenschaftlichen Tagung der Österreichischen Gesellschaft für Psychologie,* April 30th, 2006.

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